FILE 'USPAT' ENTERED AT 14:09:36 ON 06 FEB 1998

```
 ********************************
 *      WELCOME TO THE          *
 *   U.S. PATENT TEXT FILE      *
 ********************************
```

=> e radin, d/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	RADIN, ALEXANDER/IN
E2	USPAT	8	RADIN, BERNARD G/IN
E3	USPAT	0	--> RADIN, D/IN
E4	USPAT	1	RADIN, EDWARD/IN
E5	USPAT	2	RADIN, EDWARD J/IN
E6	USPAT	7	RADIN, GEORGE/IN
E7	USPAT	1	RADIN, JACK/IN
E8	USPAT	1	RADIN, MICHAEL G/IN
E9	USPAT	3	RADIN, NORMAN S/IN
E10	USPAT	2	RADIN, SHULAMIT/IN
E11	USPAT	1	RADIN, SHULAMITH/IN
E12	USPAT	1	RADIN, VLADIMIR I/IN

=> e cramer, c/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	CRAMER, BRUCE/IN
E2	USPAT	1	CRAMER, BUD L/IN
E3	USPAT	0	--> CRAMER, C/IN
E4	USPAT	1	CRAMER, CARL V SR/IN
E5	USPAT	2	CRAMER, CAROLE LYN/IN
E6	USPAT	2	CRAMER, CHARLES E/IN
E7	USPAT	1	CRAMER, CHARLES H/IN
E8	USPAT	1	CRAMER, CHARLES ROBERT/IN
E9	USPAT	2	CRAMER, CHARLES W/IN
E10	USPAT	1	CRAMER, CHARLOTTE/IN
E11	USPAT	2	CRAMER, CHRIS/IN
E12	USPAT	1	CRAMER, CHRISTOPH/IN

=> s e5;d 1-2 date leg ab
L1 2 "CRAMER, CAROLE LYN"/IN

L1: 1 of 2

TITLE: HMG2 promoter expression system
US PAT NO: 5,689,056 DATE ISSUED: Nov. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/550,544 DATE FILED: Nov. 7, 1995
REL-US-DATA: Continuation of Ser. No. 100,816, Aug. 2, 1993, abandoned.

US PAT NO: 5,689,056 :IMAGE AVAILABLE: L1: 1 of 2
DATE ISSUED: Nov. 18, 1997
TITLE: HMG2 promoter expression system
INVENTOR: **Carole Lyn Cramer**, Blacksburg, VA
Deborah Louise Weissenborn, Blacksburg, VA
ASSIGNEE: Virginia Tech Intellectual Properties, Inc., Blacksburg, VA (U.S. corp.)
APPL-NO: 08/550,544
DATE FILED: Nov. 7, 1995
ART-UNIT: 183
PRIM-EXMR: Elizabeth McElwain
LEGAL-REP: Pennie & Edmonds LLP

ABSTRACT:
The promoter elements of plant HMG2 HMGR genes are described. The HMG2 promoter elements are responsive to pathogen-infection, pest-infestation, wounding, or elicitor or chemical treatments. The HMG2 elements are also active in specialized tissues of the plant including pollen and mature fruits. HMG2 promoter elements and HMG2-derived promoters can be advantageously used to drive the expression of disease and pest resistance genes, whereby transgenic plants having such gene constructs would be resistant to the targeted disease and pest. In particular, the HMG2 gene expression system can be utilized in developing nematode-resistant plants. HMG2 promoter elements and HMG2-derived promoters can also be advantageously used to drive the post-harvest expression of desired gene products in plants, wherein the expression of the desired gene product is deferred until the expression is induced by mechanical wounding and/or elicitor treatment of all plant tissue shortly before, during or shortly after harvesting the plant. Further, HMG2 promoter elements and HMG2-derived promoters can also be advantageously used to drive the expression of desired gene products in plant cell cultures, wherein the expression of the desired gene product is deferred until the expression is induced by mechanical wounding or elicitor treatment.

L1: 2 of 2

TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
US PAT NO: 5,670,349 DATE ISSUED: Sep. 23, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/282,581 DATE FILED: Jul. 29, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 100,816, Aug. 2, 1993, abandoned.

US PAT NO: 5,670,349 :IMAGE AVAILABLE: L1: 2 of 2
DATE ISSUED: Sep. 23, 1997
TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
INVENTOR: **Carole Lyn Cramer**, Blacksburg, VA
Deborah Louise Weissenborn, Blacksburg, VA
ASSIGNEE: Virginia Tech Intellectual Properties, Inc., Blacksburg, VA (U.S. corp.)
APPL-NO: 08/282,581
DATE FILED: Jul. 29, 1994
ART-UNIT: 183
PRIM-EXMR: Elizabeth McElwain
LEGAL-REP: Pennie & Edmonds LLP

ABSTRACT:
The invention relates in part to plant HMG2 HMGR genes and in part to the "post-harvest" production method of producing gene product of interest in plant tissues and cultures. The HMG2 promoter elements are responsive to pathogen-infection, pest-infestation, wounding, or elicitor or chemical treatments. The HMG2 elements are also active in specialized tissues of the plant including pollen and mature fruits. HMG2 promoter elements and HMG2-derived promoters can be advantageously used to drive the expression of disease and pest resistance genes, whereby transgenic plants having such gene constructs would be resistant to the targeted disease and pest. In particular, the HMG2 gene expression system can be utilized in developing nematode resistant plants. The post-harvest production method of the invention utilizes plant tissues and cell cultures of plants or plant cells engineered with a expression construct comprising an inducible promoter, such as the HMG2 promoter, operably linked to a gene of interest. Production of the desired gene product is obtained by harvesting, followed by inducing and processing the harvested tissue or culture. The post-harvest production method may be advantageously used to produce direct or indirect gene products that are labile, volatile, toxic, hazardous, etc.

=> e oishi, k/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	OISHI, IWAO/IN
E2	USPAT	2	OISHI, JITSUO/IN
E3	USPAT	0	--> OISHI, K/IN
E4	USPAT	4	OISHI, KANEMITSU/IN
E5	USPAT	15	OISHI, KANJI/IN
E6	USPAT	5	OISHI, KATSUMI/IN
E7	USPAT	2	OISHI, KATSURO/IN
E8	USPAT	3	OISHI, KATSUYOSHI/IN
E9	USPAT	3	OISHI, KAYOKO/IN
E10	USPAT	12	OISHI, KAZUAKI/IN
E11	USPAT	1	OISHI, KAZUHIKO/IN
E12	USPAT	2	OISHI, KAZUHIRO/IN

=> e weissenborn, d/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	2	WEISSENBERGER, VOLKER/IN
E2	USPAT	1	WEISSENBORN, BERND/IN
E3	USPAT	0	--> WEISSENBORN, D/IN
E4	USPAT	2	WEISSENBORN, DEBORAH LOUISE/IN
E5	USPAT	1	WEISSENBORN, DIETER/IN
E6	USPAT	1	WEISSENBORN, GUSTAV/IN
E7	USPAT	1	WEISSENBORN, JORG/IN
E8	USPAT	2	WEISSENBORN, RICHARD K/IN
E9	USPAT	1	WEISSENBURG, PER TORSTEN/IN
E10	USPAT	1	WEISSENBURGER, EDWARD/IN
E11	USPAT	8	WEISSENBURGER, EDWARD A/IN
E12	USPAT	1	WEISSENBURGER, HELMUT WILHELM OTTO/IN

=> s e4; d 1-2 date leg ab
L2 2 "WEISSENBORN, DEBORAH LOUISE"/IN

L2: 1 of 2

TITLE: HMG2 promoter expression system
US PAT NO: 5,689,056 DATE ISSUED. Nov. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/550,544 DATE FILED: Nov. 7, 1995
REL-US-DATA: Continuation of Ser. No. 100,816, Aug. 2, 1993, abandoned.

US PAT NO: 5,689,056 :IMAGE AVAILABLE: L2: 1 of 2

DATE ISSUED: Nov. 18, 1997
TITLE: HMG2 promoter expression system
INVENTOR: Carole Lyn Cramer, Blacksburg, VA
Deborah Louise Weissenborn, Blacksburg, VA
ASSIGNEE: Virginia Tech Intellectual Properties, Inc., Blacksburg, VA (U.S. corp.)
APPL-NO: 08/550,544
DATE FILED: Nov. 7, 1995
ART-UNIT: 183
PRIM-EXMR: Elizabeth McElwain
LEGAL-REP: Pennie & Edmonds LLP

ABSTRACT:
The promoter elements of plant HMG2 HMGR genes are described. The HMG2 promoter elements are responsive to pathogen-infection, pest-infestation, wounding, or elicitor or chemical treatments. The HMG2 elements are also active in specialized tissues of the plant including pollen and mature fruits. HMG2 promoter elements and HMG2-derived promoters can be advantageously used to drive the expression of disease and pest resistance genes, whereby transgenic plants having such gene constructs would be resistant to the targeted disease and pest. In particular, the HMG2 gene expression system can be utilized in developing nematode-resistant plants. HMG2 promoter elements and HMG2-derived promoters can also be advantageously used to drive the post-harvest expression of desired gene products in plants, wherein the expression of the desired gene product is deferred until the expression is induced by mechanical wounding and/or elicitor treatment of all plant tissue shortly before, during or shortly after harvesting the plant. Further, HMG2 promoter elements and HMG2-derived promoters can also be advantageously used to drive the expression of desired gene products in plant cell cultures, wherein the expression of the desired gene product is deferred until the expression is induced by mechanical wounding or elicitor treatment.

L2: 2 of 2

TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
US PAT NO: 5,670,349 DATE ISSUED: Sep. 23, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/282,581 DATE FILED: Jul. 29, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 100,816, Aug. 2, 1993, abandoned.

US PAT NO: 5,670,349 :IMAGE AVAILABLE: L2: 2 of 2
DATE ISSUED: Sep. 23, 1997
TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
INVENTOR: Carole Lyn Cramer, Blacksburg, VA
Deborah Louise Weissenborn, Blacksburg, VA
ASSIGNEE: Virginia Tech Intellectual Properties, Inc., Blacksburg, VA (U.S. corp.)
APPL-NO: 08/282,581
DATE FILED: Jul. 29, 1994
ART-UNIT: 183
PRIM-EXMR: Elizabeth McElwain
LEGAL-REP: Pennie & Edmonds LLP

ABSTRACT:
The invention relates in part to plant HMG2 HMGR genes and in part to the "post-harvest" production method of producing gene product of interest in plant tissues and cultures. The HMG2 promoter elements are responsive to pathogen-infection, pest-infestation, wounding, or elicitor or chemical treatments. The HMG2 elements are also active in specialized tissues of the plant including pollen and mature fruits. HMG2 promoter elements and HMG2-derived promoters can be advantageously used to drive the expression of disease and pest resistance genes, whereby transgenic plants having such gene constructs would be resistant to the targeted disease and pest. In particular, the HMG2 gene expression system can be utilized in developing nematode resistant plants. The post-harvest production method of the invention utilizes plant tissues and cell cultures of plants or plant cells engineered with a expression construct comprising an inducible promoter, such as the HMG2 promoter, operably linked to a gene of interest. Production of the desired gene product is obtained by harvesting, followed by inducing and processing the harvested tissue or culture. The post-harvest production method may be advantageously used to produce direct or indirect gene products that are labile, volatile, toxic, hazardous, etc.

=> s lysosom? and ((transgen? or transform?) (p) (plant? or seed? or fruit?))
1251 LYSOSOM?
1588 TRANSGEN?
189247 TRANSFORM?
146899 PLANT?
58806 SEED?
26187 FRUIT?
3985 (TRANSGEN? OR TRANSFORM?) (P) (PLANT? OR SEED? OR FRUIT?)
L3 64 LYSOSOM? AND ((TRANSGEN? OR TRANSFORM?) (P) (PLANT? OR SEED
? O
R FRUIT?))

=> s (lysosom? or glucocerebro? or iduron?) and ((transgen? or transform?) (p) (plant? or seed? or fruit?))
1251 LYSOSOM?
95 GLUCOCEREBRO?
204 IDURON?
1588 TRANSGEN?
189247 TRANSFORM?
146899 PLANT?
58806 SEED?
26187 FRUIT?
3985 (TRANSGEN? OR TRANSFORM?) (P) (PLANT? OR SEED? OR FRUIT?)
L4 73 (LYSOSOM? OR GLUCOCEREBRO? OR IDURON?) AND ((TRANSGEN? OR T
RAN
SFORM?) (P) (PLANT? OR SEED? OR FRUIT?))

=> d l-73 leg date ab

US PAT NO: 5,705,732 :IMAGE AVAILABLE: L4: 1 of 73
DATE ISSUED: Jan. 6, 1998
TITLE: Universal donor cells
INVENTOR: Peter J. Sims, Mequon, WI
Alfred L.M. Bothwell, Guilford, CT
Eileen A. Elliot, New Haven, CT
Richard A. Flavell, Killingworth, CT
Joseph Madri, North Branford, CT
Scott Rollins, Monroe, CT
Leonard Bell, Woodbridge, CT
Stephen Squinto, Irvington, NY
ASSIGNEE: Oklahoma Medical Research Foundation, Oklahoma City, OK (U.S. corp.)
Yale University, New Haven, CT (U.S. corp.)
APPL-NO: 08/087,007
DATE FILED: Jul. 1, 1993
ART-UNIT: 184
PRIM-EXMR: Suzanne E. Ziska
LEGAL-REP: Arnall Golden & Gregory

L4: 1 of 73

TITLE: Universal donor cells
US PAT NO: 5,705,732 DATE ISSUED: Jan. 6, 1998
:IMAGE AVAILABLE:
APPL-NO: 08/087,007 DATE FILED: Jul. 1, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 906,394, Jun. 29, 1992, abandoned, and Ser. No. 271,562, Feb. 7, 1994, Pat. No. 5,573,940, which is a continuation-in-part of Ser. No. 729,926, Jul. 15, 1991, abandoned, which is a continuation-in-part of Ser. No. 365,199, Jun. 12, 1989, Pat. No. 5,135,916.

ABSTRACT:
Genetically engineered cells are provided which can serve as universal donor cells in such applications as reconstruction of vascular linings or the administration of therapeutic agents. The cells include a coding region which provides protection against complement-based lysis, i.e., hyperacute rejection. In addition, the cell's natural genome is changed so that functional proteins encoded by either the class II or both the class I and the class II major histocompatibility complex genes do not appear on the cell's surface. In this way, attack by T-cells is avoided. Optionally, the cells can include a self-destruction mechanism so that they can be removed from the host when no longer needed.

US PAT NO: 5,705,153 :IMAGE AVAILABLE: L4: 2 of 73
DATE ISSUED: Jan. 6, 1998
TITLE: Glycolipid enzyme-polymer conjugates
INVENTOR: Robert G. L. Shorr, Edison, NJ
Carl W. Gilbert, Basking Ridge, NJ
Brian M. Martin, Rockville, MD
Myung-Ok Cho, Seoul, Republic of Korea
Edward J. Ginns, Bethesda, MD
ASSIGNEE: The United States of America, as represented by The Department of Health and Human Services, Washington, DC (U.S. govt.)
APPL-NO: 08/735,961
DATE FILED: Oct. 23, 1996
ART-UNIT: 184
PRIM-EXMR: Rebecca E. Prouty

L4: 2 of 73

TITLE: Glycolipid enzyme-polymer conjugates
US PAT NO: 5,705,153 DATE ISSUED: Jan. 6, 1998
:IMAGE AVAILABLE:
APPL-NO: 08/735,961 DATE FILED: Oct. 23, 1996
REL-US-DATA: Division of Ser. No. 346,680, Nov. 30, 1994, Pat. No.

5,620,884, which is a continuation-in-part of Ser. No. 989,802, Dec. 10, 1992, abandoned.

ABSTRACT:
Conjugates containing **glucocerebrosidase** and non-antigenic polymers such as polyethylene glycol are disclosed. The conjugates circulate for extended times and have prolonged activity in vivo when compared to unmodified enzymes. The conjugates are useful in the treatment of Gaucher's Disease and have improved enzyme activity at the pH ranges associated with **lysosomal**, arterial and capillary regions.

US PAT NO: 5,693,506 :IMAGE AVAILABLE: L4: 3 of 73
DATE ISSUED: Dec. 2, 1997
TITLE: Process for protein production in plants
INVENTOR: Raymond L. Rodriguez, Davis, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/153,563
DATE FILED: Nov. 16, 1993
ART-UNIT: 183
PRIM-EXMR: David T. Fox
ASST-EXMR: Erich E. Veitenheimer
LEGAL-REP: Gary R. Fabian, Peter J. Dehlinger

L4: 3 of 73
TITLE: Process for protein production in plants
US PAT NO: 5,693,506 DATE ISSUED: Dec. 2, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/153,563 DATE FILED: Nov. 16, 1993

ABSTRACT:
This invention provides for the secretion of heterologous protein in plant systems. In particular, this invention provides for the production of heterologous proteins in plant cultu1res and seeds. Where seeds are the source of the protein, the heterologous genes are expressed during germination and isolated from a malt.

US PAT NO: 5,686,240 :IMAGE AVAILABLE: L4: 4 of 73
DATE ISSUED: Nov. 11, 1997
TITLE: Acid sphingomyelinase gene and diagnosis of Niemann-Pick disease
INVENTOR: Edward H. Schuchman, New York, NY
Robert J. Desnick, New York, NY
ASSIGNEE: Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 08/250,740
DATE FILED: May 27, 1994
ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
ASST-EXMR: Paul B. Tran

L4: 4 of 73
TITLE: Acid sphingomyelinase gene and diagnosis of Niemann-Pick disease
US PAT NO: 5,686,240 DATE ISSUED: Nov. 11, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/250,740 DATE FILED: May 27, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 695,572, May 3, 1991.

ABSTRACT:
The present invention relates to the acid sphingomyelinase gene and to methods of diagnosing Niemann-Pick disease. It is based, at least in part, on the cloning and expression of the full-length cDNA encoding acid sphingomyelinase, the cloning and characterization of the genomic structure of the acid sphingomyelinase gene, and on the discovery of frequent mutations in the acid sphingomyelinase gene of Ashkenazi Jewish Niemann-Pick disease patients.

US PAT NO: 5,679,343 :IMAGE AVAILABLE: L4: 5 of 73
DATE ISSUED: Oct. 21, 1997
TITLE: Bacillus thuringiensis cryET4 and cryET5 protein insecticidal composition and method of use
INVENTOR: William P. Donovan, Levittown, PA
Yuping Tan, Falls Township, PA
Christine S. Jany, Doylestown, PA
Jose M. Gonzalez, Jr., Ewing Township, NJ
ASSIGNEE: Monsanto Company, St. Louis, MO (U.S. corp.)
APPL-NO: 08/474,038
DATE FILED: Jun. 7, 1995
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Panitch Schwarze Jacobs & Nadel, P.C.

L4: 5 of 73
TITLE: Bacillus thuringiensis cryET4 and cryET5 protein insecticidal composition and method of use
US PAT NO: 5,679,343 DATE ISSUED: Oct. 21, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/474,038 DATE FILED: Jun. 7, 1995
REL-US-DATA: Division of Ser. No. 176,865, Dec. 30, 1993, which is a division of Ser. No. 100,709, Jul. 29, 1993, Pat. No. 5,322,687.

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated B.t. strain EG5847, exhibits insecticidal activity against lepidopteran insects. Two novel toxin genes from B.t. strain EG5847 designated cryET4 and cryET5 produce insecticidal proteins with activity against a broad spectrum of insects of the order Lepidoptera. The cryET4 gene has a nucleotide base sequence shown in FIG. 1 and listed in SEQ ID NO:1 and produces a CryET4 gene product having the deduced amino acid sequence shown in FIG. 1 and listed in SEQ ID NO:2. The cryET5 gene has a nucleotide base sequence shown in FIG. 2 and listed in SEQ ID NO:3 and produces a CryET5 gene product having the deduced amino acid sequence shown in FIG. 2 and listed in SEQ ID NO:4.

US PAT NO: 5,674,898 :IMAGE AVAILABLE: L4: 6 of 73
DATE ISSUED: Oct. 7, 1997
TITLE: Methods and therapeutic compositions for treating cystic fibrosis
INVENTOR: Seng Hing Cheng, Wellesley, MA
Shaona Lee Fang, Sudbury, MA
Henry Hoppe, IV, Acton, MA
Alan Edward Smith, Dover, MA
ASSIGNEE: Genzyme Corporation, Cambridge, MA (U.S. corp.)
APPL-NO: 08/072,708
DATE FILED: Jun. 7, 1993
ART-UNIT: 129
PRIM-EXMR: Peter O'Sullivan

L4: 6 of 73
TITLE: Methods and therapeutic compositions for treating cystic fibrosis
US PAT NO: 5,674,898 DATE ISSUED: Oct. 7, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/072,708 DATE FILED: Jun. 7, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 935,603, Aug. 26, 1992, abandoned, which is a continuation-in-part of Ser. No. 613,592, Nov. 15, 1990, abandoned(76) Ser. No. 589,295, Sep. 27, 1990, abandoned, which is a continuation-in-part of Ser. No. 488,307, Mar. 5, 1990, abandoned.

ABSTRACT:
Methods and compositions for treating Cystic Fibrosis by mobilizing mutant forms of CFTR, which retain at least some functional activity, to the plasma membrane where they can mediate chloride ion transport are disclosed.

US PAT NO: 5,674,747 :IMAGE AVAILABLE: L4: 7 of 73
DATE ISSUED: Oct. 7, 1997
TITLE: Viral vector coding for juvenile hormone esterase
INVENTOR: Bruce D. Hammock, Davis, CA
Terry N. Hanzlik, Chapman, Australia
Lawrence G. Harshman, Dixon, CA
Bryony C. Bonning, Davis, CA
Vernon K. Ward, Davis, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/440,520
DATE FILED: May 12, 1995
ART-UNIT: 189
PRIM-EXMR: John L. LeGuyader
LEGAL-REP: Majestic, Parsons, Siebert & Hsue

L4: 7 of 73
TITLE: Viral vector coding for juvenile hormone esterase
US PAT NO: 5,674,747 DATE ISSUED: Oct. 7, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/440,520 DATE FILED: May 12, 1995
REL-US-DATA: Division of Ser. No. 927,851, Aug. 10, 1992, Pat. No. 5,643,776, which is a continuation-in-part of Ser. No. 725,226, Jun. 26, 1991, abandoned, which is a continuation of Ser. No. 265,507, Nov. 1, 1988, abandoned.

ABSTRACT:
A diagnostic or control composition is useful to characterize or control insects and comprises a nucleotide sequence coding for juvenile hormone esterase (JHE). The coding sequence may be combined with a promoter sequence regulating the transcription thereof in a recombinant expression vector for use in controlling insects having a juvenile hormone esterase dependency. Preferred embodiments of the invention are recombinant baculoviruses in which a mutated JHE coding sequence provides relatively

rapid speed of kill in insects.

US PAT NO: 5,660,827 :IMAGE AVAILABLE: L4: 8 of 73
DATE ISSUED: Aug. 26, 1997
TITLE: Antibodies that bind to endoglin
INVENTOR: Philip E. Thorpe, Dallas, TX
Francis J. Burrows, San Diego, CA
ASSIGNEE: Board of Regents, The University of Texas System, Austin, TX (U.S. corp.)
APPL-NO: 08/457,229
DATE FILED: Jun. 1, 1995
ART-UNIT: 186
PRIM-EXMR: Lila Feisee
ASST-EXMR: Ray F. Ebert
LEGAL-REP: Arnold, White & Durkee

L4: 8 of 73
TITLE: Antibodies that bind to endoglin
US PAT NO: 5,660,827 DATE ISSUED: Aug. 26, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/457,229 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 350,212, Dec. 5, 1994, which is a continuation-in-part of Ser. No. 205,330, Mar. 2, 1994, which is a continuation-in-part of Ser. No. 295,868, Sep. 6, 1994, which is a continuation-in-part of Ser. No. 846,349, Mar. 5, 1992, abandoned.

ABSTRACT:
Disclosed are antibodies that specifically bind to endoglin. Conjugates of the antibodies linked to diagnostic or therapeutic agents are also provided. Methods of using the antibodies and conjugates are also disclosed, including methods of targeting the vasculature of solid tumors through recognition of the tumor vasculature-associated antigen, endoglin.

US PAT NO: 5,658,773 :IMAGE AVAILABLE: L4: 9 of 73
DATE ISSUED: Aug. 19, 1997
TITLE: Tomato acid invertase gene
INVENTOR: Alan B. Bennett, Davis, CA
Ellen M. Klann, Davis, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/296,624
DATE FILED: Aug. 26, 1994
ART-UNIT: 183
PRIM-EXMR: Che S. Chereskin
LEGAL-REP: Townsend and Townsend and Crew LLP

L4: 9 of 73
TITLE: Tomato acid invertase gene
US PAT NO: 5,658,773 DATE ISSUED: Aug. 19, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/296,624 DATE FILED: Aug. 26, 1994
REL-US-DATA: Continuation of Ser. No. 770,970, Oct. 7, 1991, abandoned.

ABSTRACT:
The present invention relates generally to methods for modifying the sucrose content of fruit. In particular, it relates to methods for increasing fruit sucrose content by inhibiting the expression of acid invertase. Additionally, it relates to methods for decreasing fruit sucrose content and increasing fruit hexose content by over expressing acid invortase.

US PAT NO: 5,654,168 :IMAGE AVAILABLE: L4: 10 of 73
DATE ISSUED: Aug. 5, 1997
TITLE: Tetracycline-inducible transcriptional activator and tetracycline-regulated transcription units
INVENTOR: Hermann Bujard, Heidelberg, Federal Republic of Germany
Manfred Gossen, Berkeley, CA
ASSIGNEE: BASF Aktiengesellschaft, Ludwigshafen, Federal Republic of Germany (foreign corp.)
Knoll Aktiengesellschaft, Ludwigshafen, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/275,876
DATE FILED: Jul. 15, 1994
ART-UNIT: 185
PRIM-EXMR: George C. Elliott
ASST-EXMR: John S. Brusca
LEGAL-REP: Giulio A. DeConti, Jr.

L4: 10 of 73
TITLE: Tetracycline-inducible transcriptional activator and tetracycline-regulated transcription units
US PAT NO: 5,654,168 DATE ISSUED: Aug. 5, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/275,876 DATE FILED: Jul. 15, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 270,637, Jul. 1, 1994, abandoned.

ABSTRACT:
Nucleic acid molecules and proteins useful for regulating the expression of genes in eukaryotic cells and organisms in an inducible manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is stimulated by a transcriptional activator fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences in the presence of tetracycline or a tetracycline analogue and a second polypeptide which directly or indirectly activates transcription in eukaryotic cells. In one embodiment, the fusion protein comprises a mutated Tet repressor operatively linked to a transcriptional activation polypeptide, such as a portion of herpes simplex virus virion protein 16. In the absence of an inducing agent (tetracycline or a tetracycline analogue), transcription of the tet operator-linked nucleotide sequence remains uninduced. In the presence of the inducing agent, transcription of the tet operator-linked nucleotide sequence is stimulated by the transactivator fusion protein of the invention. Novel transcription units which allow for coordinate or independent tetracycline-regulated expression of two or more nucleotide sequences by the transactivator fusion protein of the invention are also disclosed. Kits including the components of the regulatory system of the invention are also encompassed by the invention.

US PAT NO: 5,650,413 :IMAGE AVAILABLE: L4: 11 of 73
DATE ISSUED: Jul. 22, 1997
TITLE: Derivatives of swainsonine, processes for their preparation and their use as therapeutic agents
INVENTOR: Jeremy Carver, Toronto, Canada
Rajan Shah, Toronto, Canada
ASSIGNEE: Glycodesign Inc., Toronto, CA (U.S. corp.)
APPL-NO: 08/474,077
DATE FILED: Jun. 7, 1995
ART-UNIT: 123
PRIM-EXMR: Bernard Dentz
LEGAL-REP: Bereskin & Parr

L4: 11 of 73
TITLE: Derivatives of swainsonine, processes for their preparation and their use as therapeutic agents
US PAT NO: 5,650,413 DATE ISSUED: Jul. 22, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/474,077 DATE FILED: Jun. 7, 1995

ABSTRACT:
The invention relates to novel mannosidase inhibitors, processes for their preparation and their use as therapeutic agents. The invention also relates to pharmaceutical compositions containing the compounds and their use as therapeutics.

US PAT NO: 5,650,307 :IMAGE AVAILABLE: L4: 12 of 73
DATE ISSUED: Jul. 22, 1997
TITLE: Production of heterologous proteins in plants and plant cells
INVENTOR: Peter Christiaan Sijmons, Amsterdam, Netherlands
Andreas Hoekema, Oegstgeest, Netherlands
Bernardus Martinus M. Dekker, Gouda, Netherlands
Barbara Schrammeijer, Rotterdam, Netherlands
Teunis Cornelius Verwoerd, Leiden, Netherlands
Peturs Josephus M. Van Den Elzen, Voorhout, Netherlands
ASSIGNEE: Mogen International, n.v., Leiden, Netherlands (foreign corp.)
APPL-NO: 08/469,856
DATE FILED: Jun. 6, 1995
ART-UNIT: 184
PRIM-EXMR: Charles C. P. Rories
LEGAL-REP: Morrison & Foerster LLP

L4: 12 of 73
TITLE: Production of heterologous proteins in plants and plant cells
US PAT NO: 5,650,307 DATE ISSUED: Jul. 22, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/469,856 DATE FILED: Jun. 6, 1995
FRN-PR. NO: 8901932 FRN FILED: Jul. 26, 1989
FRN-PR. CO: Netherlands
FRN-PR. NO: PCT/NL90/00108 FRN FILED: Jul. 26, 1990
FRN-PR. CO: World Intellectual Property Organization
REL-US-DATA: Continuation of Ser. No. 659,287, May 21, 1991.

ABSTRACT:
This invention provides for a method to produce excreted and correctly processed heterologous protein-material in a **plant** host. The method comprises the step of **transforming** a **plant** host using a recombinant polynucleotide, which comprises the DNA sequences encoding the fully processed heterologous protein material, directly preceded by a DNA sequence coding for a **plant** signal peptide, and regulatory sequences necessary for the **plant** host to express the heterologous

gene construct, resulting in excretion of the heterologous protein from the cell and correct cleavage of the N-terminal signal peptide, so that the mature heterologous protein produced by the **plant** host is identical to the corresponding protein produced in its authentic host.

US PAT NO: 5,646,023 :IMAGE AVAILABLE: L4: 13 of 73
DATE ISSUED: Jul. 8, 1997
TITLE: Modulation of sugar content in plants
INVENTOR: Gary A. Secor, Fargo, ND
Alexander Y. Borovkov, Fargo, ND
Phillip E. McClean, Fargo, ND
Joseph R. Sowokinos, Grand Forks, ND
ASSIGNEE: J.R. Simplot Company, Boise, ID (U.S. corp.)
North Dakota State University of Agriculture and Applied Sciences, Bismarck, ND (U.S. corp.)
APPL-NO: 08/545,228
DATE FILED: Oct. 19, 1995
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody
LEGAL-REP: Townsend and Townsend and Crew LLP

L4: 13 of 73
TITLE: Modulation of sugar content in plants
US PAT NO: 5,646,023 DATE ISSUED: Jul. 8, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/545,228 DATE FILED: Oct. 19, 1995
REL-US-DATA: Continuation of Ser. No. 48,027, Apr. 15, 1993, abandoned.

ABSTRACT:
The present invention provides novel **transgenic** **plants** with altered sugar levels and methods for producing them. The methods comprise introducing into the **plant** an expression cassette comprising a promoter sequence operably linked to a polynucleotide sequence substantially identical to a sequence from a gene encoding a protein associated with sucrose biosynthesis.

US PAT NO: 5,643,776 :IMAGE AVAILABLE: L4: 14 of 73
DATE ISSUED: Jul. 1, 1997
TITLE: Insect diagnostic and control compositions
INVENTOR: Bruce D. Hammock, Davis, CA
Terry N. Hanzlik, Chapman, Australia
Lawrence G. Harshman, Dixon, CA
Bryony C. Bonning, Davis, CA
Vernon K. Ward, Davis, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 07/927,851
DATE FILED: Aug. 10, 1992
ART-UNIT: 189
PRIM-EXMR: John LeGuyader
LEGAL-REP: Majestic, Parsons, Siebert & Hsue

L4: 14 of 73
TITLE: Insect diagnostic and control compositions
US PAT NO: 5,643,776 DATE ISSUED: Jul. 1, 1997
:IMAGE AVAILABLE:
APPL-NO: 07/927,851 DATE FILED: Aug. 10, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 725,226, Jun. 26, 1991, abandoned, which is a continuation of Ser. No. 265,507, Nov. 1, 1988, abandoned.

ABSTRACT:
A diagnostic or control composition is useful to characterize or control insects and comprises a nucleotide sequence coding for juvenile hormone esterase (JHE). The coding sequence may be combined with a promoter sequence regulating the transcription thereof in a recombinant expression vector for use in controlling insects having a juvenile hormone esterase dependency. Preferred embodiments of the invention are recombinant baculoviruses in which a mutated JHE coding sequence provides relatively rapid speed of kill in insects.

US PAT NO: 5,631,153 :IMAGE AVAILABLE: L4: 15 of 73
DATE ISSUED: May 20, 1997
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
INVENTOR: Mario R. Capecchi, Salt Lake City, UT
Kirk R. Thomas, Salt Lake City, UT
ASSIGNEE: University of Utah, Salt Lake City, UT (U.S. corp.)
APPL-NO: 08/463,813
DATE FILED: Jun. 5, 1995
ART-UNIT: 184
PRIM-EXMR: Bruce R. Campell
LEGAL-REP: Townsend & Townsend & Crew LLP

L4: 15 of 73
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
US PAT NO: 5,631,153 DATE ISSUED: May 20, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/463,813 DATE FILED: Jun. 5, 1995
REL-US-DATA: Continuation of Ser. No. 14,083, Feb. 4, 1993, Pat. No. 5,464,764, which is a continuation of Ser. No. 397,707, Aug. 22, 1989, abandoned.

ABSTRACT:
Positive-negative selector (PNS) vectors are provided for modifying a target DNA sequence contained in the genome of a target cell capable of homologous recombination. The vector comprises a first DNA sequence which contains at least one sequence portion which is substantially homologous to a portion of a first region of a target DNA sequence. The vector also includes a second DNA sequence containing at least one sequence portion which is substantially homologous to another portion of a second region of a target DNA sequence. A third DNA sequence is positioned between the first and second DNA sequences and encodes a positive selection marker which when expressed is functional in the target cell in which the vector is used. A fourth DNA sequence encoding a negative selection marker, also functional in the target cell, is positioned 5' to the first or 3' to the second DNA sequence and is substantially incapable of homologous recombination with the target DNA sequence. The invention also includes **transformed** cells containing at least one predetermined modification of a target DNA sequence contained in the genome of the cell. In addition, the invention includes organisms such as non-human **transgenic** animals and **plants** which contain cells having predetermined modifications of a target DNA sequence in the genome of the organism.

US PAT NO: 5,627,059 :IMAGE AVAILABLE: L4: 16 of 73
DATE ISSUED: May 6, 1997
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
INVENTOR: Mario R. Capecchi, Salt Lake City, UT
Kirk R. Thomas, Salt Lake City, UT
ASSIGNEE: University of Utah, Salt Lake City, UT (U.S. corp.)
APPL-NO: 08/461,827
DATE FILED: Jun. 5, 1995
ART-UNIT: 184
PRIM-EXMR: Bruce R. Campbell
LEGAL-REP: Townsend & Townsend & Crew LLP

L4: 16 of 73
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
US PAT NO: 5,627,059 DATE ISSUED: May 6, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/461,827 DATE FILED: Jun. 5, 1995
REL-US-DATA: Continuation of Ser. No. 84,741, Jun. 28, 1993, Pat. No. 5,487,994, which is a division of Ser. No. 14,083, Feb. 4, 1993, Pat. No. 5,464,764, which is a continuation of Ser. No. 397,707, Aug. 22, 1989, abandoned.

ABSTRACT:
Positive-negative selector (PNS) vectors are provided for modifying a target DNA sequence contained in the genome of a target cell capable of homologous recombination. The vector comprises a first DNA sequence which contains at least one sequence portion which is substantially homologous to a portion of a first region of a target DNA sequence. The vector also includes a second DNA sequence containing at least one sequence portion which is substantially homologous to another portion of a second region of a target DNA sequence. A third DNA sequence is positioned between the first and second DNA sequences and encodes a positive selection marker which when expressed is functional in the target cell in which the vector is used. A fourth DNA sequence encoding a negative selection marker, also functional in the target cell, is positioned 5' to the first or 3' to the second DNA sequence and is substantially incapable of homologous recombination with the target DNA sequence. The invention also includes **transformed** cells containing at least one predetermined modification of a target DNA sequence contained in the genome of the cell. In addition, the invention includes organisms such as non-human **transgenic** animals and **plants** which contain cells having predetermined modifications of a target DNA sequence in the genome of the organism.

US PAT NO: 5,620,884 :IMAGE AVAILABLE: L4: 17 of 73
DATE ISSUED: Apr. 15, 1997
TITLE: Glycolipid enzyme-polymer conjugates
INVENTOR: Robert G. L. Shorr, Edison, NJ
Myung-Ok Cho, Highland Park, NJ
Carl W. Gilbert, Basking Ridge, NJ
Edward J. Ginns, Bethesda, MD
Brian M. Martin, Rockville, MD
ASSIGNEE: Enzon, Inc., Piscataway, NJ (U.S. corp.)

APPL-NO: 08/346,680
DATE FILED: Nov. 30, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Michael N. Mercanti

L4: 17 of 73

TITLE: Glycolipid enzyme-polymer conjugates
US PAT NO: 5,620,884 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/346,680 DATE FILED: Nov. 30, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 989,802, Dec. 10, 1992, abandoned.

ABSTRACT:
Conjugates containing **glucocerebrosidase** and non-antigenic polymers such as polyethylene glycol are disclosed. The conjugates circulate for extended times and have prolonged activity in vivo when compared to unmodified enzymes. The conjugates are useful in the treatment of Gaucher's Disease and have improved enzyme activity at the pH ranges associated with **lysosomal**, arterial and capillary regions.

US PAT NO: 5,616,319 :IMAGE AVAILABLE: L4: 18 of 73
DATE ISSUED: Apr. 1, 1997
TITLE: Bacillus thuringiensis cryET5 gene and related plasmids, bacteria and insecticides
INVENTOR: William P. Donovan, Levittown, PA
Yuping Tan, Falls Township, PA
Christine S. Jany, Doylestown, PA
Jos e M. Gonz alez, Jr., Ewing Township, NJ
ASSIGNEE: Monsanto Company, St. Louis, MO (U.S. corp.)
APPL-NO: 08/176,865
DATE FILED: Dec. 30, 1993
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Panitch Schwarze Jacobs & Nadel, P.C.

L4: 18 of 73

TITLE: Bacillus thuringiensis cryET5 gene and related plasmids, bacteria and insecticides
US PAT NO: 5,616,319 DATE ISSUED: Apr. 1, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/176,865 DATE FILED: Dec. 30, 1993
REL-US-DATA: Division of Ser. No. 100,709, Jul. 29, 1993, Pat. No. 5,322,687.

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated B.t. strain EG5847, exhibits insecticidal activity against lepidopteran insects. Two novel toxin genes from B.t. strain EG5847 designated cryET4 and cryET5 produce insecticidal proteins with activity against a broad spectrum of insects of the order Lepidoptera. The cryET4 gene has a nucleotide base sequence shown in FIG. 1 and listed in SEQ ID NO:1 and produces a CryET4 gene product having the deduced amino acid sequence shown in FIG. 1 and listed in SEQ ID NO:2. The cryET5 gene has a nucleotide base sequence shown in FIG. 2 and listed in SEQ ID NO:3 and produces a CryET5 gene product having the deduced amino acid sequence shown in FIG. 2 and listed in SEQ ID NO:4.

US PAT NO: 5,614,399 :IMAGE AVAILABLE: L4: 19 of 73
DATE ISSUED: Mar. 25, 1997
TITLE: Plant ubiquitin promoter system
INVENTOR: Peter H. Quail, Richmond, CA
Alan H. Christensen, Albany, CA
Howard P. Hershey, West Chester, PA
Robert A. Sharrock, El Cerrito, CA
Thomas D. Sullivan, Madsion, WI
ASSIGNEE: Mycogen Plant Science, Inc., San Diego, CA (U.S. corp.)
APPL-NO: 08/462,092
DATE FILED: Jun. 5, 1995
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody
LEGAL-REP: Saliwanchik, Lloyd & Saliwanchik

L4: 19 of 73

TITLE: Plant ubiquitin promoter system
US PAT NO: 5,614,399 DATE ISSUED: Mar. 25, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/462,092 DATE FILED: Jun. 5, 1995
REL-US-DATA: Division of Ser. No. 296,268, Aug. 25, 1994, Pat. No. 5,510,474, which is a continuation of Ser. No. 191,134, Feb. 3, 1994, abandoned, which is a continuation of Ser. No. 76,363, Jun. 11, 1993, abandoned, which is a continuation of Ser. No. 670,496, Mar. 15, 1991, abandoned, which is a continuation of Ser. No. 194,824, May 17, 1988, abandoned.

ABSTRACT:
A method of inducibly enhancing the constitutive expression of a DNA sequence of interest is described in which **plant** cells are **transformed** with a DNA sequence of interest that is operably joined to a **plant** ubiquitin regulatory region comprised of a heat shock element, a promoter, a transcription start site, an intron, and a translation start site. When monocot or dicot **plant** cells are subjected to permissive heat shock temperatures, the level of expression of the DNA sequence of interest is enhanced.

US PAT NO: 5,612,209 :IMAGE AVAILABLE: L4: 20 of 73
DATE ISSUED: Mar. 18, 1997
TITLE: Cloning and recombinant production of vespid venom phospholipases, and immunological therapies based thereon
INVENTOR: Te P. King, New York, NY
ASSIGNEE: The Rockefeller University, New York, NY (U.S. corp.)
APPL-NO: 08/385,745
DATE FILED: Feb. 8, 1995
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Tekchand Saidha
LEGAL-REP: Klauber & Jackson

L4: 20 of 73

TITLE: Cloning and recombinant production of vespid venom phospholipases, and immunological therapies based thereon
US PAT NO: 5,612,209 DATE ISSUED: Mar. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/385,745 DATE FILED: Feb. 8, 1995
REL-US-DATA: Continuation of Ser. No. 31,400, Mar. 11, 1993, abandoned.

ABSTRACT:
The present invention is directed to nucleic acids encoding vespid venom phospholipases, or fragments thereof, recombinant vectors comprising such nucleic acids, and host cells containing the recombinant vectors. The invention is further directed to expression of such nucleic acids to produce recombinant vespid venom phospholipases, or recombinant fragments, derivatives or analogs thereof. Such recombinant products are useful for diagnosis of allergy and for therapeutic treatment of allergy. In specific embodiments, the present invention provides nucleic acids encoding, and complete nucleotide and amino acids sequences for, vespid venom phospholipase A1, for example, Dolichovespula maculata phospholipase A.sub.1 and Vespula vulgaris phospholipase A1.

US PAT NO: 5,608,147 :IMAGE AVAILABLE: L4: 21 of 73
DATE ISSUED: Mar. 4, 1997
TITLE: tfdA gene selectable markers in plants and the use thereof
INVENTOR: Bryan J. Kaphammer, 1921 Ravens Crest Dr., Plainsboro, NJ 08536
APPL-NO: 08/358,117
DATE FILED: Dec. 15, 1994
ART-UNIT: 183
PRIM-EXMR: Douglas W. Robinson
ASST-EXMR: Elizabeth F. McElwain
LEGAL-REP: Dechert Price & Rhoads

L4: 21 of 73

TITLE: tfdA gene selectable markers in plants and the use thereof
US PAT NO: 5,608,147 DATE ISSUED: Mar. 4, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/358,117 DATE FILED: Dec. 15, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 179,667, Jan. 11, 1994, abandoned.

ABSTRACT:
The present invention relates, in general, to **transgenic** **plant** cells and **plants**. In particular, the present invention relates to 1) a method of selecting for a **transgenic** **plant** cell comprising **transforming** one or more **plant** cells with a tfdA gene; 2) a **plant** cell comprising a tfdA gene wherein said **plant** cell is free of other foreign marker genes; and 3) a sweetgum **plant** cell comprising a tfdA gene.

US PAT NO: 5,595,884 :IMAGE AVAILABLE: L4: 22 of 73
DATE ISSUED: Jan. 21, 1997
TITLE: Papillomavirus E2 transactivation repressor proteins and DNA
INVENTOR: Elliot J. Androphy, Natick, MA
James G. Barsoum, Lexington, MA
ASSIGNEE: Biogen Inc., Cambridge, MA (U.S. corp.)
New England Medical Center Hospitals, Inc., Boston, MA (U.S. corp.)
APPL-NO: 08/094,128
DATE FILED: Sep. 24, 1993

ART-UNIT: 182
PRIM-EXMR: Stephen G. Walsh
LEGAL-REP: James F. Haley, Jr., Madge R. Kanter

L4: 22 of 73

TITLE: Papillomavirus E2 transactivation repressor proteins and DNA
US PAT NO: 5,595,884 DATE ISSUED: Jan. 21, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/094,128 DATE FILED: Sep. 24, 1993
PCT-NO: PCT/US92/00652 PCT-FILED: Jan. 28, 1992
371-DATE: Sep. 24, 1993
102(E)-DATE: Sep. 24, 1993
PCT-PUB-NO: WO92/12728 PCT-PUB-DATE: Aug. 6, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 646,998, Jan. 28, 1991, Pat. No. 5,219,990.

ABSTRACT:

This invention relates to E2 trans-activation repressors which interfere with normal functioning of the native full-length E2 transcriptional activation protein of the papillomavirus. This invention also relates to DNA sequences and recombinant DNA molecules encoding such repressors, unicellular hosts transformed with such DNA molecules, and processes for producing and using such repressors. Native full-length E2 trans-activation protein activates transcription of papillomavirus only through binding to DNA, and it binds to DNA only in the form of a pre-formed homodimer--a pair of identical polypeptide subunits held together by non-covalent interactions. The E2 trans-activation repressors of this invention are proteins, polypeptides or other molecules that dimerize with full-length native E2 polypeptides to form inactive heterodimers, thus interfering with the formation of active homodimers comprising full-length native E2 polypeptides, thereby repressing papillomavirus transcription and replication. The E2 trans-activation repressors of this invention are advantageously used in the treatment of papillomavirus infections and their associated diseases.

US PAT NO: 5,589,362 :IMAGE AVAILABLE: L4: 23 of 73
DATE ISSUED: Dec. 31, 1996
TITLE: Tetracycline regulated transcriptional modulators with altered DNA binding specificities
INVENTOR: Hermann Bujard, Heidelberg, Federal Republic of Germany
Manfred Gossen, El Cerrito, Federal Republic of Germany
Wolfgang Hillen, Erlangen, Federal Republic of Germany
Vera Helbl, Fuerth, Federal Republic of Germany
Dirk Schnappinger, Bad Driburg, Federal Republic of Germany
ASSIGNEE: BASF Aktiengesellschaft, Ludwigshafen, Federal Republic of Germany (foreign corp.)
Knoll Aktiengesellschaft, Ludwigshafen, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/485,971
DATE FILED: Jun. 7, 1995
ART-UNIT: 185
PRIM-EXMR: George C. Elliott
ASST-EXMR: John S. Brusca
LEGAL-REP: Giulio A. DeConti, Jr.

L4: 23 of 73

TITLE: Tetracycline regulated transcriptional modulators with altered DNA binding specificities
US PAT NO: 5,589,362 DATE ISSUED: Dec. 31, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/485,971 DATE FILED: Jun. 7, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 383,754, Feb. 3, 1995, and a continuation-in-part of Ser. No. 275,876, Jul. 15, 1994, and a continuation-in-part of Ser. No. 260,452, Jun. 14, 1994, and a continuation-in-part of Ser. No. 76,726, Jun. 14, 1993, Pat. No. 5,464,758, said Ser. No. 275,876 is a continuation-in-part of Ser. No. 270,637, Jul. 1, 1994, abandoned, said Ser. No. 260,452 is a continuation-in-part of Ser. No. 76,327, Jun. 14, 1993, abandoned.

ABSTRACT:
Isolated nucleic acid molecules encoding fusion proteins which regulate transcription in eukaryotic cells are disclosed. The fusion proteins of the invention comprise a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells. Methods for regulating transcription of a tet operator-linked gene in a cell are also provided. In one embodiment, the method involves introducing into the cell a nucleic acid molecule encoding a fusion protein which regulates transcription, the fusion protein comprising a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells, and modulating the concentration of a tetracycline, or analogue thereof, in contact with the cell.

US PAT NO: 5,585,545 :IMAGE AVAILABLE: L4: 24 of 73
DATE ISSUED: Dec. 17, 1996
TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
INVENTOR: Alan B. Bennett, Davis, CA
Robert L. Fischer, El Cerrito, CA
Coralie Lashbrook, Dixon, CA
James Giovannoni, Ithaca, NY
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/271,883
DATE FILED: Jul. 7, 1994
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Townsend and Townsend and Crew LLP

L4: 24 of 73

TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
US PAT NO: 5,585,545 DATE ISSUED: Dec. 17, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/271,883 DATE FILED: Jul. 7, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 687,466, Apr. 18, 1991, Pat. No. 5,328,999, which is a continuation-in-part of Ser. No. 511,417, Apr. 20, 1990, Pat. No. 5,168,064.

ABSTRACT:
The present invention provides a method for reducing fruit softening and cell wall polysaccharide degradation by inhibiting endo-1,4-.beta.-glucanase activity using antisense nucleic acid constructions.

US PAT NO: 5,580,757 :IMAGE AVAILABLE: L4: 25 of 73
DATE ISSUED: Dec. 3, 1996
TITLE: Cloning and expression of biologically active .alpha.-galactosidase A as a fusion protein
INVENTOR: Robert J. Desnick, New York, NY
David F. Bishop, New York, NY
Yiannis A. Ioannou, New York, NY
ASSIGNEE: The Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 08/261,577
DATE FILED: Jun. 17, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith D. Hendricks
LEGAL-REP: Pennie & Edmonds

L4: 25 of 73

TITLE: Cloning and expression of biologically active .alpha.-galactosidase A as a fusion protein
US PAT NO: 5,580,757 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/261,577 DATE FILED: Jun. 17, 1994
REL-US-DATA: Division of Ser. No. 983,451, Nov. 30, 1992, Pat. No. 5,401,650, which is a continuation-in-part of Ser. No. 602,824, Oct. 24, 1990, Pat. No. 5,356,804, and Ser. No. 602,608, Oct. 24, 1990, Pat. No. 5,382,524.

ABSTRACT:
The present invention involves the production of large quantities of human .alpha.-Gal A by cloning and expressing the .alpha.-Gal A coding sequence in eukaryotic host cell expression systems. The eukaryotic expression systems, and in particular the mammalian host cell expression system described herein provide for the appropriate cotranslational and posttranslational modifications required for proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced. In addition, the expression of fusion proteins which simplify purification is described.
Using the methods described herein, the recombinant .alpha.-Gal A is secreted by the engineered host cells so that it is recovered from the culture medium in good yield. The .alpha.-Gal A produced in accordance with the invention may be used, but is not limited to, in the treatment in Fabry Disease; for the hydrolysis of .alpha.-galactosyl residues in glycoconjugates; and/or for the conversion of the blood group B antigen on erythrocytes to the blood group O antigen.

US PAT NO: 5,567,602 :IMAGE AVAILABLE: L4: 26 of 73
DATE ISSUED: Oct. 22, 1996
TITLE: Recombinant production of chymase
INVENTOR: James M. Clark, San Mateo, CA
Kevin R. Shoemaker, San Francisco, CA
Robert L. Warne, San Francisco, CA
ASSIGNEE: Arris Pharmaceutical Corporation, South San Francisco, CA (U.S. corp.)
APPL-NO: 07/929,198
DATE FILED: Aug. 12, 1992

ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Pennie & Edmonds

L4: 26 of 73

TITLE: Recombinant production of chymase
US PAT NO: 5,567,602 DATE ISSUED: Oct. 22, 1996
:IMAGE AVAILABLE:
APPL-NO: 07/929,198 DATE FILED: Aug. 12, 1992

ABSTRACT:
The instant invention is directed to recombinant production of functionally active chymase. "Functionally active" as used herein refers to the ability to exhibit one or more functional activities of a full-length wild-type chymase protein. In a preferred aspect, a proteolytically inactive chymase fusion protein comprising a functionally active portion of a non-chymase protein joined to the amino-terminus of the chymase protein is produced, which, upon cleavage away of the non-chymase fusion protein portion, becomes proteolytically active. A refolding procedure for increasing yields of proteolytically active recombinant chymase is provided. The invention is further directed to use of the recombinant chymase thus produced for preparing chymase-specific antibodies.

US PAT NO: 5,563,246 :IMAGE AVAILABLE: L4: 27 of 73
DATE ISSUED: Oct. 8, 1996
TITLE: Sodium ion binding proteins
INVENTOR: Terry A. Krulwich, New York, NY
D. Mack Ivey, Fayetteville, AR
ASSIGNEE: Mount Sinai School Of Medicine Of The City of New York, New York, NY (U.S. corp.)
APPL-NO: 08/306,062
DATE FILED: Sep. 9, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Hyosuk Kim
LEGAL-REP: Pennie & Edmonds

L4: 27 of 73

TITLE: Sodium ion binding proteins
US PAT NO: 5,563,246 DATE ISSUED: Oct. 8, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/306,062 DATE FILED: Sep. 9, 1994
REL-US-DATA: Division of Ser. No. 938,188, Aug. 28, 1992, Pat. No. 5,346,815.

ABSTRACT:
The present invention relates to the cloning and expression of a sodium ion binding protein. In particular, the invention relates to cloning and expression of a nhaS gene. The nhaS gene product, NhaS, is a protein characterized by binding to and sequestering sodium ion (Na.sup.+). The invention further relates to functional fragments of a sodium ion binding protein, which fragments are characterized by their ability to bind to sodium ion. In a specific embodiment, the fragment is a fragment of NhaS. The gene encoding the sodium binding protein can be introduced into cells to produce desalination bioreactors. The gene encoding the sodium binding protein can also be introduced into **plants** as a **transgene** to produce **plants** that are resistant to sodium. The sodium binding protein itself may be used for treatments involving Na.sup.+ /K.sup.+ ATPase disorders, e.g., in heart disease; the protein also may be introduced parenterally, preferably orally, to bind to and sequester dietary sodium.

US PAT NO: 5,554,743 :IMAGE AVAILABLE: L4: 28 of 73
DATE ISSUED: Sep. 10, 1996
TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
INVENTOR: Alan B. Bennett, Davis, CA
Robert L. Fischer, El Cerrito, CA
Coralie Lashbrook, Dixon, CA
James Giovannoni, Ithaca, NY
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/434,702
DATE FILED: May 4, 1995
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Townsend and Townsend and Crew

L4: 28 of 73

TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
US PAT NO: 5,554,743 DATE ISSUED: Sep. 10, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/434,702 DATE FILED: May 4, 1995
REL-US-DATA: Division of Ser. No. 271,883, Apr. 7, 1994, which is a continuation-in-part of Ser. No. 687,446, Apr. 18, 1991, Pat. No. 5,328,999, and a continuation-in-part of Ser. No. 511,417, Apr. 20, 1990, Pat. No. 5,168,064.

ABSTRACT:
The present invention provides a method for reducing fruit softening and cell wall polysaccharide degradation by inhibiting endo-1,4-.beta.-glucanase activity using antisense nucleic acid constructions.

US PAT NO: 5,545,815 :IMAGE AVAILABLE: L4: 29 of 73
DATE ISSUED: Aug. 13, 1996
TITLE: Control of fruit ripening in plants
INVENTOR: Robert L. Fischer, El Cerrito, CA
Linda J. Margossian, El Cerrito, CA
Lola Penarrubia, Valencia, Spain
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 07/772,032
DATE FILED: Oct. 8, 1991
ART-UNIT: 183
PRIM-EXMR: Mary E. Mosher
LEGAL-REP: Townsend and Townsend and Crew

L4: 29 of 73

TITLE: Control of fruit ripening in plants
US PAT NO: 5,545,815 DATE ISSUED: Aug. 13, 1996
:IMAGE AVAILABLE:
APPL-NO: 07/772,032 DATE FILED: Oct. 8, 1991

ABSTRACT:
The present invention provides novel **transgenic** **plants** comprising antisense DNA constructs which inhibit expression of ethylene perception genes. The **plants** exhibit decreased levels of ethylene-mediated responses, such as **fruit** ripening.

US PAT NO: 5,541,110 :IMAGE AVAILABLE: L4: 30 of 73
DATE ISSUED: Jul. 30, 1996
TITLE: Cloning and expression of a gene encoding bryodin 1 from Bryonia dioica
INVENTOR: Clay B. Siegall, Edmonds, WA
ASSIGNEE: Bristol-Myers Squibb, New York, NY (U.S. corp.)
APPL-NO: 08/245,754
DATE FILED: May 17, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Kawai Lau

L4: 30 of 73

TITLE: Cloning and expression of a gene encoding bryodin 1 from Bryonia dioica
US PAT NO: 5,541,110 DATE ISSUED: Jul. 30, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/245,754 DATE FILED: May 17, 1994

ABSTRACT:
The molecular cloning and expression of biologically active ribosome-inactivating protein bryodin 1 are described. A complete amino acid and oligonucleotide sequence encoding bryodin 1 are also described. Further, plasmids, expression vectors comprising a nucleotide sequence encoding bryodin 1 and transformed host cells are described. Isolation and characterization of the nucleotide sequence for bryodin 1 enables the recombinant production of large amount of bryodin 1 for use in vitro or in vivo directly or as ligand/toxin conjugates or fusion proteins. These compositions can be used to selectively kill undesired cells such as cancer cells, infected cells, bacteria.

US PAT NO: 5,530,187 :IMAGE AVAILABLE: L4: 31 of 73
DATE ISSUED: Jun. 25, 1996
TITLE: **Transgenic** **plants** containing multiple disease resistance genes
INVENTOR: Christopher J. Lamb, San Diego, CA
Qun Zhu, San Diego, CA
Eileen A. Maher, Madison, WI
Richard A. Dixon, Ardmore, OK
ASSIGNEE: The Salk Institute for Biological Studies, La Jolla, CA (U.S. corp.)
APPL-NO: 08/093,372
DATE FILED: Jul. 16, 1993
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Stephen E. Reiter, Robert T. Ramos

L4: 31 of 73

TITLE: **Transgenic** **plants** containing multiple disease resistance genes
US PAT NO: 5,530,187 DATE ISSUED: Jun. 25, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/093,372 DATE FILED: Jul. 16, 1993

ABSTRACT:

In accordance with the present invention, there are provided **transgenic** **plants** comprising a plurality of **plant**-defense-associated proteins that are expressed to produce such proteins in an amount sufficient to increase the **plants** resistance to **plant** pathogens, relative to non-**transgenic** **plants** of the same species. The **transgenic** **plants** are useful to study patterns of development, and to provide increased resistance to **plant** pathogens when grown in crops as a food source, and the like. Nucleic acid constructs are also provided that are useful in methods for producing the invention **transgenic** **plants**.

US PAT NO: 5,527,695 :IMAGE AVAILABLE: L4: 32 of 73
DATE ISSUED: Jun. 18, 1996
TITLE: Controlled modification of eukaryotic genomes
INVENTOR: Thomas K. Hodges, West Lafayette, IN
Leszek A. Lyznik, West Lafayette, IN
ASSIGNEE: Purdue Research Foundation, West Lafayette, IN (U.S. corp.)
APPL-NO: 08/010,997
DATE FILED: Jan. 29, 1993
ART-UNIT: 183
PRIM-EXMR: David T. Fox
ASST-EXMR: Erich E. Veitenheimer
LEGAL-REP: Barnes & Thornburg

L4: 32 of 73
TITLE: Controlled modification of eukaryotic genomes
US PAT NO: 5,527,695 DATE ISSUED: Jun. 18, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/010,997 DATE FILED: Jan. 29, 1993

ABSTRACT:
DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs allow a more precise and effective transformation procedure by enabling the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.

US PAT NO: 5,525,713 :IMAGE AVAILABLE: L4: 33 of 73
DATE ISSUED: Jun. 11, 1996
TITLE: DNA encoding polypeptides enabling sorting of proteins to vacuoles in plants
INVENTOR: Natasha V. Raikhel, Okemos, MI
ASSIGNEE: Board of Trustees operating Michigan State University, East Lansing, MI (U.S. corp.)
APPL-NO: 08/173,515
DATE FILED: Dec. 23, 1993
ART-UNIT: 183
PRIM-EXMR: Mary E. Mosher
LEGAL-REP: Ian C. McLeod

L4: 33 of 73
TITLE: DNA encoding polypeptides enabling sorting of proteins to vacuoles in plants
US PAT NO: 5,525,713 DATE ISSUED: Jun. 11, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/173,515 DATE FILED: Dec. 23, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 917,665, Jul. 20, 1992, Pat. No. 5,276,269, which is a continuation-in-part of Ser. No. 406,318, Sep. 12, 1989, abandoned, and a continuation-in-part of Ser. No. 791,930, Nov. 12, 1991, Pat. No. 5,360,726, which is a continuation-in-part of Ser. No. 612,200, Nov. 13, 1990, abandoned, which is a continuation-in-part of Ser. No. 406,318, Sep. 12, 1989, abandoned.

ABSTRACT:
A DNA encoding a polypeptide enabling sorting of proteins to vacuoles in plants, particularly tobacco is described. Without this sequence, the protein is not sorted to the vacuoles. The polypeptide is attached to the C-terminal region of the protein and is particularly useful for sorting of lectins to the vacuole which are insecticidal.

US PAT NO: 5,516,694 :IMAGE AVAILABLE: L4: 34 of 73
DATE ISSUED: May 14, 1996
TITLE: Endo-xyloglucan transferase
INVENTOR: Kazuhiko Nishitani, Kagoshima, Japan
Kazuhide Okazawa, Otsu, Japan
Kiyozo Asada, Shiga, Japan
Ikunoshin Kato, Uji, Japan
ASSIGNEE: Takara Shuzo Co., Ltd., Kyoto, Japan (foreign corp.)
APPL-NO: 08/381,280
DATE FILED: Jan. 31, 1995
ART-UNIT: 184
PRIM-EXMR: Christopher S. F. Low
LEGAL-REP: Wenderoth, Lind & Ponack

L4: 34 of 73
TITLE: Endo-xyloglucan transferase
US PAT NO: 5,516,694 DATE ISSUED: May 14, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/381,280 DATE FILED: Jan. 31, 1995
FRN-PR. NO: 4-098506 FRN FILED: Mar. 26, 1992
FRN-PR. CO: Japan
FRN-PR. NO: 4-217489 FRN FILED: Jul. 24, 1992
FRN-PR. CO: Japan
FRN-PR. NO: 5-031163 FRN FILED: Jan. 28, 1993
FRN-PR. CO: Japan
REL-US-DATA: Continuation of Ser. No. 37,281, Mar. 26, 1993, abandoned, which is a continuation-in-part of Ser. No. 929,513, Aug. 14, 1992, abandoned.

ABSTRACT:
Endo-xyloglucan transferases responsible for growth of plant cell wall, genes coding for the enzymes, a method of transferring xyloglucan molecules by using the enzyme, and methods of using the gene are described.

US PAT NO: 5,516,657 :IMAGE AVAILABLE: L4: 35 of 73
DATE ISSUED: May 14, 1996
TITLE: Baculovirus vectors for expression of secretory and membrane-bound proteins
INVENTOR: Cheryl I. Murphy, Hopkinton, MA
Elihu Young, Sharon, MA
ASSIGNEE: Cambridge Biotech Corporation, Worcester, MA (U.S. corp.)
APPL-NO: 08/029,402
DATE FILED: Mar. 5, 1993
ART-UNIT: 185
PRIM-EXMR: Mindy B. Fleisher
ASST-EXMR: David Guzo
LEGAL-REP: Sterne, Kessler, Goldstein & Fox

L4: 35 of 73
TITLE: Baculovirus vectors for expression of secretory and membrane-bound proteins
US PAT NO: 5,516,657 DATE ISSUED: May 14, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/029,402 DATE FILED: Mar. 5, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 880,647, May 11, 1992, abandoned.

ABSTRACT:
The invention provides Baculovirus vectors comprised of a promoter upstream from a signal peptide. The Baculovirus vectors allow for the expression of a glycosylated protein in the late term of Baculovirus infection. Methods for the construction of such a Baculovirus vector are also provided. In addition, methods for producing large amounts of a desired glycosylated protein in the late term infection of Baculovirus infection are also provided.

US PAT NO: 5,510,474 :IMAGE AVAILABLE: L4: 36 of 73
DATE ISSUED: Apr. 23, 1996
TITLE: Plant ubiquitin promoter system
INVENTOR: Peter H. Quail, Richmond, CA
Alan H. Christensen, Albany, CA
Howard P. Hershey, West Chester, PA
Robert A. Sharrock, El Cerrito, CA
Thomas D. Sullivan, Madison, WI
ASSIGNEE: Mycogen Plant Science, Inc., San Diego, CA (U.S. corp.)
APPL-NO: 08/296,268
DATE FILED: Aug. 25, 1994
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody
LEGAL-REP: Saliwanchik & Saliwanchik

L4: 36 of 73
TITLE: Plant ubiquitin promoter system
US PAT NO: 5,510,474 DATE ISSUED: Apr. 23, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/296,268 DATE FILED: Aug. 25, 1994
REL-US-DATA: Continuation of Ser. No. 191,134, Feb. 3, 1994, abandoned, which is a continuation of Ser. No. 76,363, Jun. 11, 1993, abandoned, which is a continuation of Ser. No. 670,496, Mar. 15, 1991, abandoned, which is a continuation of Ser. No. 194,824, May 17, 1988, abandoned.

ABSTRACT:
A DNA segment from the upstream untranscribed region of a maize ubiquitin gene is disclosed. This ubiquitin promoter region, which comprises heat shock consensus elements, initiates and regulates the transcription of genes placed under its control. Recombinant DNA molecules are also described in which a ubiquitin promoter is combined with a plant expressible structural gene for regulated expression of the structural

gene and for regulated control of expression when stressed with elevated temperatures. Such recombinant DNA molecules are introduced into plant tissue so that the promoter/structural gene combination is expressed.

US PAT NO: 5,501,969 :IMAGE AVAILABLE: L4: 37 of 73
DATE ISSUED: Mar. 26, 1996
TITLE: Human osteoclast-derived cathepsin
INVENTOR: Gregg A. Hastings, Rockville, MD
Mark D. Adams, Potomac, MD
Claire M. Fraser, Gueenstown, MD
Norman H. Lee, Woodstock, MD
Ewen F. Kirkness, Washington, DC
Judith A. Blake, Laurel, MD
Lisa M. Fitzgerald, Germantown, MD
Fred H. Drake, Glenmoore, PA
Maxine Gowan, Valley Forge, PA
ASSIGNEE: Human Genome Sciences, Inc., Rockville, MD (U.S. corp.)
APPL-NO: 08/208,007
DATE FILED: Mar. 8, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Eric Grimes
LEGAL-REP: Elliot M. Olstein, Gregory D. Ferraro

L4: 37 of 73
TITLE: Human osteoclast-derived cathepsin
US PAT NO: 5,501,969 DATE ISSUED: Mar. 26, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/208,007 DATE FILED: Mar. 8, 1994

ABSTRACT:
Disclosed is a human osteoclast-derived cathepsin (Cathepsin O) polypeptide and DNA(RNA) encoding such cathepsin O polypeptides. Also provided is a procedure for producing such polypeptide by recombinant techniques. The present invention also discloses antibodies, antagonists and inhibitors of such polypeptide which may be used to prevent the action of such polypeptide and therefore may be used therapeutically to treat bone diseases such as osteoporosis and cancers, such as tumor metastases.

US PAT NO: 5,491,075 :IMAGE AVAILABLE: L4: 38 of 73
DATE ISSUED: Feb. 13, 1996
TITLE: Cloning and expression of biologically active .alpha.-N-acetylgalactosaminidase
INVENTOR: Robert J. Desnick, New York, NY
David F. Bishop, New York, NY
Yiannis A. Ioannou, New York, NY
Anne M. Wang, New York, NY
ASSIGNEE: The Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 08/261,578
DATE FILED: Jun. 17, 1994
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith D. Hendricks
LEGAL-REP: Pennie & Edmonds

L4: 38 of 73
TITLE: Cloning and expression of biologically active .alpha.-N-acetylgalactosaminidase
US PAT NO: 5,491,075 DATE ISSUED: Feb. 13, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/261,578 DATE FILED: Jun. 17, 1994
REL-US-DATA: Division of Ser. No. 602,608, Oct. 24, 1990, Pat. No. 5,382,524.

ABSTRACT:
The present invention involves the production of human .alpha.-GalNAc by cloning and expressing the .alpha.-GalNAc coding sequence in eukaryotic host cell expressions systems. The eukaryotic expression systems, and in particular the mammalian host cell expression systems described herein provide for the appropriate co-translational and post-translation modifications required or proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced.
The .alpha.-GalNAc produced in accordance with the invention may be used in the treatment of Schindler disease or for the hydrolysis of .alpha.-N-acetylgalactosaminyl moieties in various glycoconjugates.

US PAT NO: 5,487,992 :IMAGE AVAILABLE: L4: 39 of 73
DATE ISSUED: Jan. 30, 1996
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
INVENTOR: Mario R. Capecchi, Salt Lake City, UT
Kirk R. Thomas, Salt Lake City, UT
ASSIGNEE: University of Utah Research Foundation, Salt Lake City, UT (U.S. corp.)
APPL-NO: 08/084,741
DATE FILED: Jun. 28, 1993
ART-UNIT: 184
PRIM-EXMR: Jacqueline M. Stone
ASST-EXMR: Bruce R. Campell
LEGAL-REP: Townsend and Townsend and Crew

L4: 39 of 73
TITLE: Cells and non-human organisms containing predetermined genomic modifications and positive-negative selection methods and vectors for making same
US PAT NO: 5,487,992 DATE ISSUED: Jan. 30, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/084,741 DATE FILED: Jun. 28, 1993
REL-US-DATA: Division of Ser. No. 14,083, Feb. 4, 1993, which is a continuation of Ser. No. 397,707, Aug. 22, 1989, abandoned.

ABSTRACT:
Positive-negative selector (PNS) vectors are provided for modifying a target DNA sequence contained in the genome of a target cell capable of homologous recombination. The vector comprises a first DNA sequence which contains at least one sequence portion which is substantially homologous to a portion of a first region of a target DNA sequence. The vector also includes a second DNA sequence containing at least one sequence portion which is substantially homologous to another portion of a second region of a target DNA sequence. A third DNA sequence is positioned between the first and second DNA sequences and encodes a positive selection marker which when expressed is functional in the target cell in which the vector is used. A fourth DNA sequence encoding a negative selection marker, also functional in the target cell, is positioned 5' to the first or 3' to the second DNA sequence and is substantially incapable of homologous recombination with the target DNA sequence. The invention also includes **transformed** cells containing at least one predetermined modification of a target DNA sequence contained in the genome of the cell. In addition, the invention includes organisms such as non-human **transgenic** animals and **plants** which contain cells having predetermined modifications of a target DNA sequence in the genome of the organism.

US PAT NO: 5,482,852 :IMAGE AVAILABLE: L4: 40 of 73
DATE ISSUED: Jan. 9, 1996
TITLE: Biologically safe **plant** **transformation** system
INVENTOR: John I. Yoder, Winters, CA
Michael W. Lassner, Davis, CA
ASSIGNEE: Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/077,787
DATE FILED: Jun. 15, 1993
ART-UNIT: 183
PRIM-EXMR: Gary Benzion
LEGAL-REP: Townsend and Townsend and Crew

L4: 40 of 73
TITLE: Biologically safe **plant** **transformation** system
US PAT NO: 5,482,852 DATE ISSUED: Jan. 9, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/077,787 DATE FILED: Jun. 15, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 555,271, Jul. 19, 1990, Pat. No. 5,225,341.

ABSTRACT:
This invention relates to methods for producing **transgenic** **plants** that contain a gene of interest and that are free of foreign ancillary nucleic acids. These methods allow for the production of **plants** which thus contain a desired gene, but which are free of vector sequences and/or marker sequences used to **transform** the **plant**. The method of **transforming** such **plants** calls for **transforming** the **plants** with a gene of interest by introduction of the gene on a DNA construct comprising a transposon and foreign ancillary nucleic acids; crossing the **transformed** **plant** through self-crossing or with another **plant** to obtain F.sub.1 or more removed generation progeny; and utilizing a means for selecting those progeny that carry the gene of interest and are free of the ancillary nucleic acids. Such progeny may be detected biochemically, by Southern hybridization, through the use of polymerase chain reaction procedures and other methods available in the art.

US PAT NO: 5,472,939 :IMAGE AVAILABLE: L4: 41 of 73
DATE ISSUED: Dec. 5, 1995
TITLE: Method of treating complement mediated disorders
INVENTOR: Douglas T. Fearon, Baltimore, MD
Lloyd B. Klickstein, Brookline, MA
Winnie W. Wong, Newton, MA
Gerald R. Carson, Wellesley, MA
Michael F. Concino, Newton, MA
Stephen H. Ip, Sudbury, MA

Savvas C. Makrides, Bedford, MA
Henry C. Marsh, Jr., Reading, MA
ASSIGNEE: The Johns Hopkins University, Baltimore, MD (U.S. corp.)
The Brigham and Women's Hospital, Boston, MA (U.S. corp.)
T Cell Sciences, Inc., Needham, MA (U.S. corp.)
APPL-NO: 08/138,825
DATE FILED: Oct. 19, 1993
ART-UNIT: 182
PRIM-EXMR: Garnette D. Draper
ASST-EXMR: John D. Ulm
LEGAL-REP: Pennie & Edmonds

L4: 41 of 73

TITLE: Method of treating complement mediated disorders
US PAT NO: 5,472,939 DATE ISSUED: Dec. 5, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/138,825 DATE FILED: Oct. 19, 1993
REL-US-DATA: Division of Ser. No. 588,128, Sep. 24, 1990, Pat. No. 5,256,642, which is a continuation-in-part of Ser. No. 412,745, Sep. 26, 1989, abandoned, which is a continuation-in-part of Ser. No. 332,865, Apr. 3, 1989, Pat. No. 5,212,071, which is a continuation-in-part of Ser. No. 176,532, Apr. 1, 1988, abandoned.

ABSTRACT:
The present invention relates to the C3b/C4b receptor (CR1) gene and its encoded protein. The invention also relates to CR1 nucleic acid sequences and fragments thereof comprising 70 nucleotides and their encoded peptides or proteins comprising 24 amino acids. The invention further provides for the expression of the CR1 protein and fragments thereof. The genes and proteins of the invention have uses in diagnosis and therapy of disorders involving complement activity, and various immune system or inflammatory disorders. In specific embodiments of the present invention detailed in the examples sections infra, the cloning, nucleotide sequence, and deduced amino acid sequence of a full-length CR1 cDNA and fragments thereof are described. The expression of the CR1 protein and fragments thereof is also described. Also described is the expression of a secreted CR1 molecule lacking a transmembrane region. The secreted CR1 molecule is shown to be useful in reducing damage caused by inflammation and in reducing myocardial infarct size and preventing reperfusion injury.

US PAT NO: 5,464,764 :IMAGE AVAILABLE: L4: 42 of 73
DATE ISSUED: Nov. 7, 1995
TITLE: Positive-negative selection methods and vectors
INVENTOR: Mario R. Capecchi, Salt Lake City, UT
Kirk R. Thomas, Salt Lake City, UT
ASSIGNEE: University of Utah Research Foundation, Salt Lake City, UT (U.S. corp.)
APPL-NO: 08/014,083
DATE FILED: Feb. 4, 1993
ART-UNIT: 184
PRIM-EXMR: Jacqueline M. Stone
ASST-EXMR: Bruce Campbell
LEGAL-REP: Townsend and Townsend Khourie and Crew

L4: 42 of 73

TITLE: Positive-negative selection methods and vectors
US PAT NO: 5,464,764 DATE ISSUED: Nov. 7, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/014,083 DATE FILED: Feb. 4, 1993
REL-US-DATA: Continuation of Ser. No. 397,707, Aug. 22, 1989, abandoned.

ABSTRACT:
Positive-negative selector (PNS) vectors are provided for modifying a target DNA sequence contained in the genome of a target cell capable of homologous recombination. The vector comprises a first DNA sequence which contains at least one sequence portion which is substantially homologous to a portion of a first region of a target DNA sequence. The vector also includes a second DNA sequence containing at least one sequence portion which is substantially homologous to another portion of a second region of a target DNA sequence. A third DNA sequence is positioned between the first and second DNA sequences and encodes a positive selection marker which when expressed is functional in the target cell in which the vector is used. A fourth DNA sequence encoding a negative selection marker, also functional in the target cell, is positioned 5' to the first or 3' to the second DNA sequence and is substantially incapable of homologous recombination with the target DNA sequence. The invention also includes **transformed** cells containing at least one predetermined modification of a target DNA sequence contained in the genome of the cell. In addition, the invention includes organisms such as non-human **transgenic** animals and **plants** which contain cells having predetermined modifications of a target DNA sequence in the genome of the organism.

US PAT NO: 5,422,274 :IMAGE AVAILABLE: L4: 43 of 73
DATE ISSUED: Jun. 6, 1995
TITLE: Internal deletion mutants of soluble T4(CD4)
INVENTOR: Paul J. Maddon, New York, NY
Richard Axel, New York, NY
Raymond W. Sweet, Bala Cynwyd, PA
James Arthos, Ann Arbor, MI
ASSIGNEE: The Trustees of Columbia University in the City of New York, New York, NY (U.S. corp.)
SmithKline Beckman Corporation, Philadelphia, PA (U.S. corp.)
APPL-NO: 07/830,489
DATE FILED: Feb. 5, 1992
ART-UNIT: 186
PRIM-EXMR: George C. Elliott
ASST-EXMR: T. Michael Nisbet
LEGAL-REP: John P. White

L4: 43 of 73

TITLE: Internal deletion mutants of soluble T4(CD4)
US PAT NO: 5,422,274 DATE ISSUED: Jun. 6, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/830,489 DATE FILED: Feb. 5, 1992
REL-US-DATA: Division of Ser. No. 160,348, Feb. 24, 1988, Pat. No. 5,110,906, which is a continuation of Ser. No. 114,244, Oct. 23, 1987, Pat. No. 5,126,443, which is a continuation-in-part of Ser. No. 898,587, Aug. 21, 1986, abandoned.

ABSTRACT:
This invention provides a therapeutic agent capable of specifically forming a complex with human immunodeficiency virus envelope glycoprotein which comprises a polypeptide. In one embodiment of the invention, the amino acid sequence of the polypeptide has the amino acid sequence shown in FIG. 6 from about +1 to about +185 fused to the amino acid sequence from about +353 to about +371. In another embodiment of the invention, the amino acid sequence of the polypeptide has the amino acid sequence shown in FIG. 6 from about +1 to about +106 fused to the amino acid sequence from about +353 to about +371. In yet a further embodiment of the invention, the amino acid sequence of the polypeptide has the amino acid sequence shown in FIG. 6 from about +1 to about +185.
This invention also provides a method for treating a subject infected with a human immunodeficiency virus. The method treats the subject with an effective amount of a pharmaceutical composition having an effective amount of a therapeutic agent of the invention and a pharmaceutically acceptable carrier.

US PAT NO: 5,401,650 :IMAGE AVAILABLE: L4: 44 of 73
DATE ISSUED: Mar. 28, 1995
TITLE: Cloning and expression of biologically active .alpha.-galactosidase A
INVENTOR: Robert J. Desnick, New York, NY
David F. Bishop, New York, NY
Yiannis A. Ioannou, New York, NY
ASSIGNEE: The Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 07/983,451
DATE FILED: Nov. 30, 1992
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith D. Hendricks
LEGAL-REP: Pennie & Edmonds

L4: 44 of 73

TITLE: Cloning and expression of biologically active .alpha.-galactosidase A
US PAT NO: 5,401,650 DATE ISSUED: Mar. 28, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/983,451 DATE FILED: Nov. 30, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 602,824, Oct. 24, 1990, and Ser. No. 602,608, Oct. 24, 1990.

ABSTRACT:
The present invention involves the production of large quantities of human .alpha.-Gal A by cloning and expressing the .alpha.-Gal A coding sequence in eukaryotic host cell expression systems. The eukaryotic expression systems, and in particular the mammalian host cell expression system described herein provide for the appropriate cotranslational and posttranslational modifications required for proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced. In addition, the expression of fusion proteins which simplify purification is described.
Using the methods described herein, the recombinant .alpha.-Gal A is secreted by the engineered host cells so that it is recovered from the culture medium in good yield. The .alpha.-Gal A produced in accordance with the invention may be used, but is not limited to, in the treatment in Fabry Disease; for the hydrolysis of .alpha.-galactosyl residues in glycoconjugates; and/or for the conversion of the blood group B antigen on erythrocytes to the blood group O antigen.

US PAT NO: 5,382,524 :IMAGE AVAILABLE: L4: 45 of 73
DATE ISSUED: Jan. 17, 1995
TITLE: Cloning and expression of biologically active .alpha.-n-acetylgalactosaminidase
INVENTOR: Robert J. Desnick, New York, NY
David F. Bishop, New York, NY
Yiannis A. Ioannou, New York, NY
Anne M. Wang, New York, NY
ASSIGNEE: The Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 07/602,608
DATE FILED: Oct. 24, 1990
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith D. Hendricks
LEGAL-REP: Pennie & Edmonds

L4: 45 of 73

TITLE: Cloning and expression of biologically active .alpha.-n-acetylgalactosaminidase
US PAT NO: 5,382,524 DATE ISSUED: Jan. 17, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/602,608 DATE FILED: Oct. 24, 1990

ABSTRACT:
The present invention involves the production of human .alpha.-GalNAc by cloning and expressing the .alpha.-GalNAc coding sequence in eukaryotic host cell expressions systems. The eukaryotic expression systems, and in particular the mammalian host cell expression systems described herein provide for the appropriate co-translational and post-translation modifications required or proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced.
The .alpha.-GalNAc produced in accordance with the invention may be used in the treatment of Schindler disease or for the hydrolysis of .alpha.-N-acetylgalactosaminyl moieties in various glycoconjugates.

US PAT NO: 5,382,429 :IMAGE AVAILABLE: L4: 46 of 73
DATE ISSUED: Jan. 17, 1995
TITLE: Bacillus thuringiensis protein toxic to coleopteran insects
INVENTOR: William P. Donovan, Levittown, PA
Mark J. Rupar, Wilmington, DE
Annette C. Slaney, Hamilton Square, NJ
Timothy B. Johnson, Langhorne, PA
ASSIGNEE: Ecogen Inc., Langhorne, PA (U.S. corp.)
APPL-NO: 07/950,352
DATE FILED: Sep. 24, 1992
ART-UNIT: 185
PRIM-EXMR: Richard A. Schwartz
ASST-EXMR: Gary L. Brown
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 46 of 73

TITLE: Bacillus thuringiensis protein toxic to coleopteran insects
US PAT NO: 5,382,429 DATE ISSUED: Jan. 17, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/950,352 DATE FILED: Sep. 24, 1992
REL-US-DATA: Division of Ser. No. 496,568, Mar. 20, 1990, Pat. No. 5,187,091.

ABSTRACT:
A purified and isolated cryIII-type gene was obtained from a novel B.t. strain. The gene has a nucleotide base sequence coding for the amino acid sequence illustrated in FIG. 1 . The 74.4 kDa protein produced by this gene is an irregularly shaped crystal that is toxic to coleopteran insects, including Colorado potato beetle and insects of the genus Diabrotica.

US PAT NO: 5,378,625 :IMAGE AVAILABLE: L4: 47 of 73
DATE ISSUED: Jan. 3, 1995
TITLE: Bacillus thuringiensis cryIIIC, (b) protein toxic to coleopteran insects
INVENTOR: William P. Donovan, Levittown, PA
Mark J. Rupar, Wilmington, DE
Annette C. Slaney, Hamilton Square, NJ
ASSIGNEE: Ecogen, Inc., Langhorne, PA (U.S. corp.)
APPL-NO: 08/113,534
DATE FILED: Aug. 27, 1993
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Hyosuk Kim
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 47 of 73

TITLE: Bacillus thuringiensis cryIIIC, (b) protein toxic to coleopteran insects
US PAT NO: 5,378,625 DATE ISSUED: Jan. 3, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/113,534 DATE FILED: Aug. 27, 1993
REL-US-DATA: Division of Ser. No. 32,775, Mar. 15, 1993, Pat. No. 5,264,364, which is a continuation of Ser. No. 813,592, Dec. 23, 1991, abandoned, which is a continuation-in-part of Ser. No. 649,562, Jan. 31, 1991.

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated EG5144, exhibits insecticidal activity against coleopteran insects, including Colorado potato beetle and insects of the genus Diabrotica. A novel toxin gene in B.t. strain EG5144 produces an irregularly shaped insecticidal crystal protein of approximately 70 kDa that is toxic to coleopteran insects. The cryIII-type gene (SEQ ID NO:1), designated as the cryIIIC(b) gene, has a nucleotide base sequence illustrated in FIG. 1.

US PAT NO: 5,360,726 :IMAGE AVAILABLE: L4: 48 of 73
DATE ISSUED: Nov. 1, 1994
TITLE: Polypeptides enabling sorting of proteins to vacuoles in plants
INVENTOR: Natasha V. Raikhel, Okemos, MI
ASSIGNEE: Board of Trustees operating Michigan State University, East Lansing, MI (U.S. corp.)
APPL-NO: 07/791,930
DATE FILED: Nov. 12, 1991
ART-UNIT: 185
PRIM-EXMR: Gary Benzion
ASST-EXMR: Mary E. Mosher
LEGAL-REP: Ian C. McLeod

L4: 48 of 73

TITLE: Polypeptides enabling sorting of proteins to vacuoles in plants
US PAT NO: 5,360,726 DATE ISSUED: Nov. 1, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/791,930 DATE FILED: Nov. 12, 1991
REL-US-DATA: Continuation-in-part of Ser. No. 612,200, Nov. 13, 1990, abandoned, which is a continuation-in-part of Ser. No. 406,318, Sep. 12, 1989, abandoned.

ABSTRACT:
A polypeptide enabling sorting of proteins to vacuoles in plants, particularly tobacco is described. The polypeptide has the sequence VFAEAIAANSTLVAE. Without this sequence, the protein is not sorted to the vacuoles. The polypeptide is attached to the C-terminal region of the protein and is particularly useful for sorting of lectins to the vacuole which are insecticidal.

US PAT NO: 5,356,804 :IMAGE AVAILABLE: L4: 49 of 73
DATE ISSUED: Oct. 18, 1994
TITLE: Cloning and expression of biologically active human .alpha.-galactosidase A
INVENTOR: Robert J. Desnick, New York, NY
David F. Bishop, New York, NY
Yiannis A. Ioannou, New York, NY
ASSIGNEE: Mount Sinai School of Medicine of the City of New York, New York, NY (U.S. corp.)
APPL-NO: 07/602,824
DATE FILED: Oct. 24, 1990
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith D. Hendricks
LEGAL-REP: Pennie & Edmonds

L4: 49 of 73

TITLE: Cloning and expression of biologically active human .alpha.-galactosidase A
US PAT NO: 5,356,804 DATE ISSUED: Oct. 18, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/602,824 DATE FILED: Oct. 24, 1990

ABSTRACT:
The present invention involves the production of large quantities of human .alpha.-Gal A by cloning and expressing the .alpha.-Gal A coding sequence in eukaryotic host cell expression systems. The eukaryotic expression systems, and in particular the mammalian host cell expression system described herein provide for the appropriate cotranslational and posttranslational modifications required for proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced. In addition, the expression of fusion proteins which simplify purification is described.
Using the methods described herein, the recombinant .alpha.-Gal A is secreted by the engineered host cells so that it is recovered from the culture medium in good yield. The .alpha.-Gal A produced in accordance with the invention may be used in the treatment in Fabry Disease; for the

hydrolysis of .alpha.-galactosyl residues in glycoconjugates; and/or for the conversion of the blood group B antigen on erythrocytes to the blood group O antigen.

US PAT NO: 5,356,623 :IMAGE AVAILABLE: L4: 50 of 73
DATE ISSUED: Oct. 18, 1994
TITLE: Bacillus thuringiensis cryET1 toxin gene and protein toxic to lepidopteran insects
INVENTOR: Michael A. von Tersch, Ewing Township, NJ
Jose M. Gonzalez, Ewing Township, NJ
ASSIGNEE: Ecogen Inc., Langhorne, PA (U.S. corp.)
APPL-NO: 08/032,364
DATE FILED: Mar. 17, 1993
ART-UNIT: 184
PRIM-EXMR: Che S. Chereskin
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 50 of 73
TITLE: Bacillus thuringiensis cryET1 toxin gene and protein toxic to lepidopteran insects
US PAT NO: 5,356,623 DATE ISSUED: Oct. 18, 1994
:IMAGE AVAILABLE:
APPL-NO: 08/032,364 DATE FILED: Mar. 17, 1993

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated EG5092, exhibits insecticidal activity against lepidopteran insects. A purified and isolated novel cryET1 toxin gene product from B.t. strain EG5092 exhibits specific insecticidal activity against Plutella xylostella (Diamondback moth). The cryET1 gene (SEQ ID NO:1) has a nucleotide base sequence illustrated in FIG. 1 and produces a CryET1 gene product (SEQ ID NO:2) having a deduced amino acid sequence illustrated in FIG. 1.

US PAT NO: 5,346,815 :IMAGE AVAILABLE: L4: 51 of 73
DATE ISSUED: Sep. 13, 1994
TITLE: Sodium ion binding proteins
INVENTOR: Terry A. Krulwich, New York, NY
D. Mack Ivey, Fayetteville, AR
ASSIGNEE: The Mount Sinai School of Medicine of the City University of New York, New York, NY (U.S. corp.)
APPL-NO: 07/938,188
DATE FILED: Aug. 28, 1992
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Hyosuk Kim
LEGAL-REP: Pennie & Edmonds

L4: 51 of 73
TITLE: Sodium ion binding proteins
US PAT NO: 5,346,815 DATE ISSUED: Sep. 13, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/938,188 DATE FILED: Aug. 28, 1992

ABSTRACT:
The present invention relates to the cloning and expression of a sodium ion binding protein. In particular, the invention relates to cloning and expression of a nhaS gene. The nhaS gene product, NhaS, is a protein characterized by binding to and sequestering sodium ion (Na.sup.+). The invention further relates to functional fragments of a sodium ion binding protein, which fragments are characterized by their ability to bind to sodium ion. In a specific embodiment, the fragment is a fragment of NhaS. The gene encoding the sodium binding protein can be introduced into cells to produce desalination bioreactors. The gene encoding the sodium binding protein can also be introduced into **plants** as a **transgene** to produce **plants** that are resistant to sodium. The sodium binding protein itself may be used for treatments involving Na.sup.+ /K.sup.+ ATPase disorders, e.g., in heart disease; the protein also may be introduced parenterally, preferably orally, to bind to and sequester dietary sodium.

US PAT NO: 5,328,999 :IMAGE AVAILABLE: L4: 52 of 73
DATE ISSUED: Jul. 12, 1994
TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
INVENTOR: Alan B. Bennett, Davis, CA
Robert L. Fischer, El Cerrito, CA
Coralie Lashbrook, Dixon, CA
James Giovannoni, Ithaca, NY
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 07/687,466
DATE FILED: Apr. 18, 1991
ART-UNIT: 184
PRIM-EXMR: David T. Fox
LEGAL-REP: Townsend and Townsend Khourie and Crew

L4: 52 of 73
TITLE: Endo-1,4-.beta.-glucanase genes and their use in plants
US PAT NO: 5,328,999 DATE ISSUED: Jul. 12, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/687,466 DATE FILED: Apr. 18, 1991
REL-US-DATA: Continuation-in-part of Ser. No. 511,417, Apr. 20, 1990, Pat. No. 5,168,064.

ABSTRACT:
The present invention provides a method for reducing fruit softening and cell wall polysaccharide degradation by inhibiting endo-1,4-.beta.-glucanase activity using antisense DNA constructions.

US PAT NO: 5,322,687 :IMAGE AVAILABLE: L4: 53 of 73
DATE ISSUED: Jun. 21, 1994
TITLE: Bacillus thuringiensis cryet4 and cryet5 toxin genes and proteins toxic to lepidopteran insects
INVENTOR: William P. Donovan, Levittown, PA
Yuping Tan, Falls Township, Bucks County, PA
Christine S. Jany, Doylestown, PA
Jose M. Gonzalez, Jr., Ewing Township, Mercer County, NJ
ASSIGNEE: Ecogen Inc., DE (U.S. corp.)
APPL-NO: 08/100,709
DATE FILED: Jul. 29, 1993
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 53 of 73
TITLE: Bacillus thuringiensis cryet4 and cryet5 toxin genes and proteins toxic to lepidopteran insects
US PAT NO: 5,322,687 DATE ISSUED: Jun. 21, 1994
:IMAGE AVAILABLE:
APPL-NO: 08/100,709 DATE FILED: Jul. 29, 1993

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated B.t. strain EG5847, exhibits insecticidal activity against lepidopteran insects. Two novel toxin genes from B.t. strain EG5847 designated cryET4 and cryET5 produce insecticidal proteins with activity against a broad spectrum of insects of the order Lepidoptera. The cryET4 gene has a nucleotide base sequence shown in FIG. 1 and listed in SEQ ID NO:1 and produces a CryET4 gene product having the deduced amino acid sequence shown in FIG. 1 and listed in SEQ ID NO:2. The cryET5 gene has a nucleotide base sequence shown in FIG. 2 and listed in SEQ ID NO:3 and produces a CryET5 gene product having the deduced amino acid sequence shown in FIG. 2 and listed in SEQ ID NO:4.

US PAT NO: 5,272,071 :IMAGE AVAILABLE: L4: 54 of 73
DATE ISSUED: Dec. 21, 1993
TITLE: Method for the modification of the expression characteristics of an endogenous gene of a given cell line
INVENTOR: Scott C. Chappel, Jamaica Plain, MA
ASSIGNEE: Applied Research Systems Ars Holding N.V., Curacao, Netherlands Antilles (foreign corp.)
APPL-NO: 07/893,447
DATE FILED: May 28, 1992
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Miguel Escallon
LEGAL-REP: Browdy and Neimark

L4: 54 of 73
TITLE: Method for the modification of the expression characteristics of an endogenous gene of a given cell line
US PAT NO: 5,272,071 DATE ISSUED: Dec. 21, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/893,447 DATE FILED: May 28, 1992
PCT-NO: PCT/US90/07642 PCT-FILED: Dec. 21, 1990
371-DATE: May 28, 1992
102(E)-DATE: May 28, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 454,783, Dec. 22, 1989, abandoned.

ABSTRACT:

Normally transcriptionally silent genes in a cell line or microorganism may be activated for expression by inserting a DNA regulatory element which is capable of promoting the expression of a normally expressed gene product in that cell or which is promiscuous, the regulatory element being inserted so as to be operatively linked with the normally silent gene in question. The insertion is accomplished by means of homologous recombination by creating a DNA construct including a segment having a DNA segment of the normally silent gene (targeting DNA) and the DNA regulatory element to induce gene transcription. The technique is also used to modify the expression characteristics of any endogenous gene of a given cell line or microorganism.

US PAT NO: 5,264,364 :IMAGE AVAILABLE: L4: 55 of 73
DATE ISSUED: Nov. 23, 1993
TITLE: Bacillus thuringiensis cryIIIc(B) toxin gene and protein toxic to coleopteran insects
INVENTOR: Willam P. Donovan, Levittown, PA
Mark J. Rupar, Wilmington, DE
Annette C. Slaney, Hamilton Square, NJ
ASSIGNEE: Ecogen Inc., Langhorne, PA (U.S. corp.)
APPL-NO: 08/032,775
DATE FILED: Mar. 15, 1993
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Hyosuk Kim
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 55 of 73

TITLE: Bacillus thuringiensis cryIIIc(B) toxin gene and protein toxic to coleopteran insects
US PAT NO: 5,264,364 DATE ISSUED: Nov. 23, 1993
:IMAGE AVAILABLE:
APPL-NO: 08/032,775 DATE FILED: Mar. 15, 1993
REL-US-DATA: Continuation of Ser. No. 813,592, Dec. 23, 1991, abandoned, which is a continuation-in-part of Ser. No. 649,562, Jan. 31, 1991, abandoned.

ABSTRACT:
A Bacillus thuringiensis strain isolate, designated EG5144, exhibits insecticidal activity against coleopteran insects, including Colorado potato beetle and insects of the genus Diabrotica. A novel toxin gene in B.t. strain EG5144 produces an irregularly shaped insecticidal crystal protein of approximately 70 kDa that is toxic to coleopteran insects. The cryIII-type gene (SEQ ID NO:1), designated as the cryIIIC(b) gene, has a nucleotide base sequence illustrated in FIG. 1.

US PAT NO: 5,256,642 :IMAGE AVAILABLE: L4: 56 of 73
DATE ISSUED: Oct. 26, 1993
TITLE: Compositions of soluble complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof
INVENTOR: Douglas T. Fearon, Baltimore, MD
Lloyd B. Klickstein, Brookline, MA
Winnie W. Wong, Newton, MA
Gerald R. Carson, Wellesley, MA
Michael F. Concino, Newton, MA
Stephen H. Ip, Sudbury, MA
Savvas; C. Makrides, Bedford, MA
Henry C. Marsh, Jr., Reading, MA
ASSIGNEE: The Johns Hopkins University, Baltimore, MD (U.S. corp.)
Brigham and Women's Hospital, Boston, MA (U.S. corp.)
T Cell Sciences, Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 07/588,128
DATE FILED: Sep. 24, 1990
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Stephen Walsh
LEGAL-REP: PenniPennie

L4: 56 of 73

TITLE: Compositions of soluble complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof
US PAT NO: 5,256,642 DATE ISSUED: Oct. 26, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/588,128 DATE FILED: Sep. 24, 1990
REL-US-DATA: Continuation-in-part of Ser. No. 412,745, Sep. 26, 1989, abandoned, which is a continuation-in-part of Ser. No. 332,865, Apr. 3, 1989, abandoned, which is a continuation-in-part of Ser. No. 176,532, Apr. 1, 1988, abandoned.

ABSTRACT:
The present invention relates to compositions comprising soluble complement receptor 1 (CR1) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention further relates to methods for treating thrombotic conditions in humans and animals by administering a composition comprising soluble CR1 and a thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

US PAT NO: 5,242,805 :IMAGE AVAILABLE: L4: 57 of 73
DATE ISSUED: Sep. 7, 1993
TITLE: Long wavelength lipophilic fluorogenic glycosidase substrates
INVENTOR: John J. Naleway, Eugene, OR
Yu-zhong Zhang, Eugene, OR
Richard P. Haugland, Eugene, OR
ASSIGNEE: Molecular Probes, Inc., Eugene, OR (U.S. corp.)
APPL-NO: 07/749,255
DATE FILED: Aug. 23, 1991
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Pamela S. Webber
LEGAL-REP: Allegra J. Helfenstein

L4: 57 of 73

TITLE: Long wavelength lipophilic fluorogenic glycosidase substrates
US PAT NO: 5,242,805 DATE ISSUED: Sep. 7, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/749,255 DATE FILED: Aug. 23, 1991

ABSTRACT:
The claimed invention relates to a substrate for evaluating glycosidic enzymes comprising a resorufin derivative of the general formula: ##STR1## wherein Gly is a carbohydrate bonded to resorufin by a glycosidic linkage; where at least one of substituents R.sub.1, R.sub.2, R.sub.4, R.sub.6, R.sub.8, and R.sub.9 is a lipophilic residue of the formula --L(CH.sub.2).sub.n CH.sub.3, where n is greater than 3 and less than 22, and where L is a methylene --CH.sub.2 --, an amide --NHCO--, a sulfonamide --NHSO.sub.2 --, a carboxamide --CONH--, a carboxylate ester --COO--, a urethane --NHCOO--, a urea --NHCONH--, or a thiourea --NHCSNH--; and
where the remainder of substituents R.sub.1, R.sub.2, R.sub.4, R.sub.6, R.sub.8, and R.sub.9, which may be the same or different, are hydrogen, halogen, or other lipophilic residues, which may be the same or different, containing from about 1 to about 22 carbon atoms of the formula --L'(CH.sub.2).sub.m CH.sub.3, where m is less than 22, and where L' is a methylene --CH.sub.2 --, an amide --NHCO--, a sulfonamide --NHSO.sub.2 --, a carboxamide --CONH--, a carboxylate ester --COO--, a urethane --NHCOO--, a urea --NHCONH--, or a thiourea --NHCSNH--. A preferred embodiment of the invention is a non-fluorescent substrate specifically hydrolyzable by a glycosidase inside a cell to yield, after greater than about 2 minutes, an orange to red fluorescent detection product which is ret

This invention was made with Government support under grant GM 38987 awarded by the National Institutes of Health. The Government has certain rights in this invention.

US PAT NO: 5,234,834 :IMAGE AVAILABLE: L4: 58 of 73
DATE ISSUED: Aug. 10, 1993
TITLE: Constructs for expression of monellin in plant cells
INVENTOR: Robert Fischer, Elcerrito, CA
Sung-Hou Kim, Moraga, CA
Joong M. Cho, Moraga, CA
Lola Penarrubia, Berkeley, CA
James Giovannoni, San Francisco, CA
Rosalind Kim, Moraga, CA
ASSIGNEE: The Regents of the University of California, Emeryville, CA (U.S. corp.)
Lucky Biotech Corp., Emeryville, CA (U.S. corp.)
APPL-NO: 07/557,222
DATE FILED: Jul. 24, 1990
ART-UNIT: 184
PRIM-EXMR: Che S. Chereskin
LEGAL-REP: Morrison & Foerster

L4: 58 of 73

TITLE: Constructs for expression of monellin in plant cells
US PAT NO: 5,234,834 DATE ISSUED: Aug. 10, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/557,222 DATE FILED: Jul. 24, 1990
FRN-PR. NO: 88905520.8 FRN FILED: May 31, 1988
FRN-PR. CO: European Patent Office
FRN-PR. NO: PCT/US88/01825 FRN FILED: May 31, 1988
FRN-PR. CO: World Intellectual Property Organization
FRN-PR. NO: 568296 FRN FILED: Jun. 1, 1988
FRN-PR. CO: Canada
FRN-PR. NO: 19940/88 FRN FILED: Jun. 17, 1988
FRN-PR. CO: Australia
FRN-PR. NO: PCT/US88/02114 FRN FILED: Jun. 17, 1988
FRN-PR. CO: World Intellectual Property Organization
FRN-PR. NO: 596926 FRN FILED: Jun. 20, 1988
FRN-PR. CO: Canada
FRN-PR. NO: 89700274 FRN FILED: Feb. 16, 1989
FRN-PR. CO: Republic of Korea
FRN-PR. NO: 89700292 FRN FILED: Feb. 18, 1989
FRN-PR. CO: Republic of Korea
REL-US-DATA: Continuation-in-part of Ser. No. 502,257, Mar. 30, 1990, which is a continuation-in-part of Ser. No. 64,341, Jun. 19, 1987, abandoned, which is a continuation-in-part of Ser. No. 64,343, Jun. 19, 1987, abandoned, and Ser. No. 117,124, Nov. 4, 1987, abandoned, which is a continuation of Ser. No. 465,585, Jan. 18, 1990, abandoned.

ABSTRACT:
Edible **fruit**, **seed** and vegetables of **transgenic** **plants** modified to produce a sweetening protein such as monellin or thaumatin are useful in preparing food compositions which have enhanced sweetness improved flavor. Expression systems for the genes encoding sweetening proteins compatible with **plant** systems and designed to enhance the production of these proteins in the edible portions of **plants**, and methods for producing sweetened **fruit**, **seeds** and vegetables are described.

US PAT NO: 5,225,341 :IMAGE AVAILABLE: L4: 59 of 73
DATE ISSUED: Jul. 6, 1993
TITLE: Biologically safe **plant** **transformation** system using a Ds transposon
INVENTOR: John I. Yoder, Davis, CA
Michael W. Lassner, Davis, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 07/555,271
DATE FILED: Jul. 19, 1990
ART-UNIT: 184
PRIM-EXMR: Che S. Chereskin
LEGAL-REP: Townsend and Townsend Khourie and Crew

L4: 59 of 73

TITLE: Biologically safe **plant** **transformation** system using a Ds transposon
US PAT NO: 5,225,341 DATE ISSUED: Jul. 6, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/555,271 DATE FILED: Jul. 19, 1990

ABSTRACT:
This invention relates to methods for producing **transgenic** **plants** that contain a gene of interest and that are free of foreign ancillary nucleic acids. These methods allow for the production of **plants** which thus contain a desired gene, but which are free of vector sequences and/or marker sequences used to **transform** the **plant**. The method of **transforming** such **plants** calls for **transforming** the **plants** with a gene of interest by introduction of the gene on a DNA construct comprising a transposon and foreign ancillary nucleic acids; crossing the **transformed** **plant** through self-crossing or with another **plant** to obtain F.sub.1 or more removed generation progeny; and utilizing a means for selecting those progeny that carry the gene of interest and are free of the ancillary nucleic acids. Such progeny may be detected biochemically, by Southern hybridization, through the use of polymerase chain reaction procedures and other methods available in the art.

US PAT NO: 5,221,620 :IMAGE AVAILABLE: L4: 60 of 73
DATE ISSUED: Jun. 22, 1993
TITLE: Cloning and expression of transforming growth factor .beta.2
INVENTOR: Anthony F. Purchio, Seattle, WA
Linda Madisen, Seattle, WA
Nancy Webb, College Station, TX
ASSIGNEE: Oncogen, Seattle, WA (U.S. corp.)
APPL-NO: 07/446,020
DATE FILED: Dec. 5, 1989
ART-UNIT: 183
PRIM-EXMR: Joan Ellis
LEGAL-REP: Pennie & Edmonds

L4: 60 of 73

TITLE: Cloning and expression of transforming growth factor .beta.2
US PAT NO: 5,221,620 DATE ISSUED: Jun. 22, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/446,020 DATE FILED: Dec. 5, 1989
REL-US-DATA: Continuation-in-part of Ser. No. 285,140, Dec. 16, 1988, abandoned, which is a continuation-in-part of Ser. No. 234,065, Aug. 18, 1988, abandoned, which is a continuation-in-part of Ser. No. 148,267, Jan. 25, 1988, abandoned, which is a continuation-in-part of Ser. No. 106,752, Oct. 6, 1987, abandoned.

ABSTRACT:
cDNA clones coding for TGF-.beta.2 which are used to construct expression vectors capable of directing the high-level expression of mature, biologically active TGF-.beta.2, as well as precursor TGF-.beta.2 forms, in transfected Chinese Hamster Ovary cells (CHO cells) and transfected COS cells are described. CHO and COS transfectants secreting TGF-.beta.2 at high levels are also described. CHO cells transfected with a plasmid vector carrying the complete 414 amino acid simian TGF-.beta.2 precursor secrete approximately 5 .mu.g per ml culture media.

US PAT NO: 5,217,902 :IMAGE AVAILABLE: L4: 61 of 73
DATE ISSUED: Jun. 8, 1993
TITLE: Method of introducing spectinomycin resistance into plants
INVENTOR: Jonathan Jones, Norwich, United Kingdom
Pal Maliga, East Brunswick, NJ
ASSIGNEE: DNA Plant Technology Corporation, Oakland, CA (U.S. corp.)
APPL-NO: 07/709,537
DATE FILED: Jun. 3, 1991
ART-UNIT: 184
PRIM-EXMR: Che S. Chereskin
LEGAL-REP: Clinton H. Neagley

L4: 61 of 73

TITLE: Method of introducing spectinomycin resistance into plants
US PAT NO: 5,217,902 DATE ISSUED: Jun. 8, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/709,537 DATE FILED: Jun. 3, 1991
REL-US-DATA: Division of Ser. No. 357,493, May 26, 1989, Pat. No. 5,073,675.

ABSTRACT:
This invention relates to the discovery that the prokaryotic enzyme, aminoglycoside 3"-adenyltransferase (AGAT), in particular as encoded by a bacterial aadA gene, is useful as a selectable marker for **transformed** **plants**. The enzyme conveys resistance to spectinomycin and streptomycin. Such markers are particularly advantageous because they are non-lethal, provide rapid visual identification of **transformed** cells and permit selection in media containing either spectinomycin or streptomycin. In addition, AGAT may be used as a selectable marker which differentiates by enabling survival on selective media.

US PAT NO: 5,212,071 :IMAGE AVAILABLE: L4: 62 of 73
DATE ISSUED: May 18, 1993
TITLE: Nucleic acids encoding a human C3b/C4b receptor (CR1)
INVENTOR: Douglas T. Fearon, Baltimore, MD
Lloyd B. Klickstein, Brookline, MA
Winnie W. Wong, Newton, MA
Gerald R. Carson, Wellesley, MA
Michael F. Concino, Newton, MA
Stephen H. Ip, Sudbury, MA
Savvas C. Makrides, Bedford, MA
ASSIGNEE: The Johns Hopkins University, Baltimore, MD (U.S. corp.)
Brigham and Women's Hospital, Boston, MA (U.S. corp.)
T Cell Sciences, Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 07/332,865
DATE FILED: Apr. 3, 1989
ART-UNIT: 182
PRIM-EXMR: David L. Lacey
ASST-EXMR: John D. Ulm

L4: 62 of 73

TITLE: Nucleic acids encoding a human C3b/C4b receptor (CR1)
US PAT NO: 5,212,071 DATE ISSUED: May 18, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/332,865 DATE FILED: Apr. 3, 1989
REL-US-DATA: Continuation-in-part of Ser. No. 176,532, Apr. 1, 1988, abandoned.

US PAT NO: 5,208,148 :IMAGE AVAILABLE: L4: 63 of 73
DATE ISSUED: May 4, 1993
TITLE: Lipophilic fluorescent glycosidase substrates
INVENTOR: Richard P. Haugland, Eugene, OR
John J. Naleway, Eugene, OR
Yu-zhong Zhang, Eugene, OR
ASSIGNEE: Molecular Probes, Inc., Eugene, OR (U.S. corp.)
APPL-NO: 07/623,600
DATE FILED: Dec. 7, 1990
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Louise Leary

L4: 63 of 73

TITLE: Lipophilic fluorescent glycosidase substrates
US PAT NO: 5,208,148 DATE ISSUED: May 4, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/623,600 DATE FILED: Dec. 7, 1990

ABSTRACT:
The claimed invention relates to a substrate for evaluating glycosidic enzymes comprising a fluorescein derivative of the general formula: ##STR1## wherein GlyX is a carbohydrate bonded to fluorescein by a glycosidic linkage;
Y, which may be the same as GlyX or different, is an alkyl ether, an ester, or a glycosidically linked carbohydrate;
R is a lipophilic residue containing from 1 to 21 carbon atoms; and
L links the R residue to fluorescein.
A preferred embodiment of the invention is a non-fluorescent substrate specifically hydrolyzable by a glycosidase inside a cell to yield, after greater than about 2 minutes, a fluorescent detection product excitable

at between about 460 nm and 550 nm and with fluorescence observable at an emission wavelength longer than the excitation wavelength, which fluorescent detection product is retained inside a viable cell more than about 2 hours at greater than about 15.degree. C. and which is non-toxic to the cell. A further embodiment of the invention is a method for evaluating a glycosidic enzyme in living plant or animal cells whether the enzyme is present endogenously; present as a result of manipulation of the cell's genome, or added to the cell exogenously, such as by covalently binding the enzyme to a protein to form an enzyme-protein complex that enters the cell.

US PAT NO: 5,187,091 :IMAGE AVAILABLE: L4: 64 of 73
DATE ISSUED: Feb. 16, 1993
TITLE: Bacillus thuringiensis cryIIIC gene encoding toxic to coleopteran insects
INVENTOR: William P. Donovan, Levittown, PA
Mark J. Rupar, Wilmington, DE
Annette C. Slaney, Hamilton Square, NJ
Timothy B. Johnson, Langhorne, PA
ASSIGNEE: Ecogen Inc., Langhorne, PA (U.S. corp.)
APPL-NO: 07/496,568
DATE FILED: Mar. 20, 1990
ART-UNIT: 185
PRIM-EXMR: Richard A. Schwartz
ASST-EXMR: John LeGuyader
LEGAL-REP: Christopher Egolf, Alan S. Nadel

L4: 64 of 73
TITLE: Bacillus thuringiensis cryIIIC gene encoding toxic to coleopteran insects
US PAT NO: 5,187,091 DATE ISSUED: Feb. 16, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/496,568 DATE FILED: Mar. 20, 1990

ABSTRACT:
A purified and isolated cryIII-type gene was obtained from a novel B.t. strain. The gene has a nucleotide base sequence coding for the amino acid sequence illustrated in FIG. 1. The 74.4 kDa protein produced by this gene is an irregularly shaped crystal that is toxic to coleopteran insects, including Colorado potato beetle and insects of the genus Diabrotica.

US PAT NO: 5,168,064 :IMAGE AVAILABLE: L4: 65 of 73
DATE ISSUED: Dec. 1, 1992
TITLE: Endo-1,4-.beta.-glucanase gene and its use in plants
INVENTOR: Alan B. Bennett, Davis, CA
Robert L. Fischer, El Cerrito, CA
Coralie Lashbrook, Dixon, CA
James Giovannoni, San Francisco, CA
ASSIGNEE: The Regents of the University of California, Oakland, CA (U.S. corp.)
APPL-NO: 07/511,417
DATE FILED: Apr. 20, 1990
ART-UNIT: 184
PRIM-EXMR: David T. Fox
LEGAL-REP: Townsend and Townsend

L4: 65 of 73
TITLE: Endo-1,4-.beta.-glucanase gene and its use in plants
US PAT NO: 5,168,064 DATE ISSUED: Dec. 1, 1992
:IMAGE AVAILABLE:
APPL-NO: 07/511,417 DATE FILED: Apr. 20, 1990

ABSTRACT:
The present invention provides a method for reducing fruit softening and cell wall polysaccharide degradation by inhibiting endo-1,4-.beta.-glucanase activity using antisense DNA constructions.

US PAT NO: 5,126,433 :IMAGE AVAILABLE: L4: 66 of 73
DATE ISSUED: Jun. 30, 1992
TITLE: Soluble forms of the T cell surface protein CD4
INVENTOR: Paul J. Maddon, New York, NY
Leonard Chess, Scarsdale, NY
Richard Axel, New York, NY
Robin Weiss, London, England
Dan R. Littman, San Francisco, CA
J. Steven McDougal, Atlanta, GA
ASSIGNEE: The Trustees of Columbia University in the City of New York, New York, NY (U.S. corp.)
APPL-NO: 07/114,244
DATE FILED: Oct. 23, 1987
ART-UNIT: 187
PRIM-EXMR: Margaret Moskowitz
ASST-EXMR: Scott A. Chambers
LEGAL-REP: John P. White

L4: 66 of 73
TITLE: Soluble forms of the T cell surface protein CD4
US PAT NO: 5,126,433 DATE ISSUED: Jun. 30, 1992
:IMAGE AVAILABLE:
APPL-NO: 07/114,244 DATE FILED: Oct. 23, 1987
REL-US-DATA: Continuation-in-part of Ser. No. 898,587, Aug. 21, 1986, abandoned.

ABSTRACT:
A single-stranded nucleic acid molecule which encodes an amino acid sequence comprising at least a portion of a T4 glycoprotein is provided. Additionally, amino acid sequences which comprise at least a portion of a T4 glycoprotein and are useful as a prophylaxis for treating a subject with acquired immune deficiency syndrome are provided. These amino acid sequences, are capable of specifically forming a complex with a human immunodeficiency virus envelope glycoprotein and which are soluble in an aqueous solution. Monoclonal antibodies directed to the water-soluble amino acid sequences of the present invention may be used as vaccines for immunizing a subject against acquired immune deficiency syndrome.

US PAT NO: 5,118,668 :IMAGE AVAILABLE: L4: 67 of 73
DATE ISSUED: Jun. 2, 1992
TITLE: Variants of bovine pancreatic trypsin inhibitor and pharmaceutical use thereof
INVENTOR: Ernst-August Auerswald, Munich, Federal Republic of Germany
Wolfgang Bruns, Wuppertal, Federal Republic of Germany
Dietrich Horlein, Wuppertal, Federal Republic of Germany
Gerd Reinhardt, Wuppertal, Federal Republic of Germany
Eugen Schnabel, Wuppertal, Federal Republic of Germany
Werner Schroder, Wuppertal, Federal Republic of Germany
ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Federal Republic of Germany (foreign corp.)
APPL-NO: 07/221,835
DATE FILED: Jul. 20, 1988
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Keith C. Furman
LEGAL-REP: Sprung Horn Kramer & Woods

L4: 67 of 73
TITLE: Variants of bovine pancreatic trypsin inhibitor and pharmaceutical use thereof
US PAT NO: 5,118,668 DATE ISSUED: Jun. 2, 1992
:IMAGE AVAILABLE:
APPL-NO: 07/221,835 DATE FILED: Jul. 20, 1988
FRN-PR. NO: 8718777 FRN FILED: Aug. 7, 1987
FRN-PR. CO: United Kingdom

ABSTRACT:
Peptides having essentially the sequence of bovine pancreatic trypsin inhibitor (aprotinin) wherein one or more of the amino acids at positions 15, 16, 17, 18, 34, 39 and 52 are replaced by any naturally occurring amino acid produced by recombinant DNA technology, process, expression vector and recominant host therefor and pharmaceutical use thereof. Such peptides being useful as therapeutic agents in diseases connected with the presence of excessive amounts of proteinases.

US PAT NO: 5,110,906 :IMAGE AVAILABLE: L4: 68 of 73
DATE ISSUED: May 5, 1992
TITLE: Derivatives of soluble T-4
INVENTOR: Paul J. Maddon, New York, NY
Richard Axel, New York, NY
Raymond W. Sweet, Bala Cynwyd, PA
James Arthos, Ann Arbor, MI
ASSIGNEE: The Trustees of Columbia University in the City of New York, New York, NY (U.S. corp.)
Smithkline Beckman Corporation, Philadelphia, PA (U.S. corp.)
APPL-NO: 07/160,348
DATE FILED: Feb. 24, 1988
ART-UNIT: 187
PRIM-EXMR: Christine Nucker
LEGAL-REP: John P. White, Antoinette F. Konski

L4: 68 of 73
TITLE: Derivatives of soluble T-4
US PAT NO: 5,110,906 DATE ISSUED: May 5, 1992
:IMAGE AVAILABLE:
APPL-NO: 07/160,348 DATE FILED: Feb. 24, 1988
REL-US-DATA: Continuation-in-part of Ser. No. 114,244, Oct. 23, 1987, which is a continuation-in-part of Ser. No. 898,587, Aug. 21, 1986, abandoned.

ABSTRACT:
This invention provides a therapeutic agent capable of specifically forming a complex with human immunodeficiency virus envelope glycoprotein which comprises a polypeptide. In one embodiment of the invention, the amino acid sequence of the polypeptide comprises the amino acid sequence

shown in FIG. 6 from about +1 to about +185 fused to the amino acid sequence from about +353 to about +371. In another embodiment of the invention, the amino acid sequence of the polypeptide comprises the amino acid sequence shown in FIG. 6 from about +1 to about +106 fused to the amino acid sequence from about +353 to about +371. In yet a further embodiment of the invention, the amino acid sequence of the polypeptide comprises the amino acid sequence shown in FIG. 6 from about +1 to about +185.

This invention also provides a method for treating a subject infected with a human immunodeficiency virus. The method comprises administering to the subject an effective amount of a pharmaceutical composition comprising an effective amount of a therapeutic agent of the invention and a pharmaceutically acceptable carrier.

US PAT NO: 5,073,675 :IMAGE AVAILABLE: L4: 69 of 73
DATE ISSUED: Dec. 17, 1991
TITLE: Method of introducing spectinomycin resistance into plants
INVENTOR: Jonathan Jones, Norwich, United Kingdom
Pal Maliga, East Bruswick, NJ
ASSIGNEE: DNA Plant Technology Corporation, Oakland, CA (U.S. corp.)
APPL-NO: 07/357,493
DATE FILED: May 26, 1989
ART-UNIT: 184
PRIM-EXMR: Elizabeth C. Weimar
ASST-EXMR: Che S. Chereskin
LEGAL-REP: Townsend and Townsend

L4: 69 of 73
TITLE: Method of introducing spectinomycin resistance into plants
US PAT NO: 5,073,675 DATE ISSUED: Dec. 17, 1991
:IMAGE AVAILABLE:
APPL-NO: 07/357,493 DATE FILED: May 26, 1989

ABSTRACT:
This invention relates to the discovery that the prokaryotic enzyme, aminoglycoside 3"-adenyltransferase (AGAT), in particular as encoded by a bacterial aadA gene, is useful as a selectable marker for **transformed** **plants**. The enzyme conveys resistance to spectinomycin and streptomycin. Such markers are particularly advantageous because they are non-lethal, provide rapid visual identification of **transformed** cells and permit selection in media containing either spectinomycin or streptomycin. In addition, AGAT may be used as a selectable marker which differentiates by enabling survival on selective media.

US PAT NO: 5,045,543 :IMAGE AVAILABLE: L4: 70 of 73
DATE ISSUED: Sep. 3, 1991
TITLE: 5-amino or substituted amino 1,2,3-triazoles useful as antimetastatic agents
INVENTOR: Donald Hupe, Westfield, NJ
ASSIGNEE: Merck & Co., Inc., Rahway, NJ (U.S. corp.)
APPL-NO: 07/348,823
DATE FILED: May 8, 1989
ART-UNIT: 125
PRIM-EXMR: Jerome D. Goldberg
LEGAL-REP: Curtis C. Panzer, Hesna J. Pfeiffer

L4: 70 of 73
TITLE: 5-amino or substituted amino 1,2,3-triazoles useful as antimetastatic agents
US PAT NO: 5,045,543 DATE ISSUED: Sep. 3, 1991
:IMAGE AVAILABLE:
APPL-NO: 07/348,823 DATE FILED: May 8, 1989
REL-US-DATA: Continuation-in-part of Ser. No. 87,494, Aug. 20, 1987, Pat. No. 4,847,257, Jul. 11, 1989.

ABSTRACT:
This invention is directed to the method of treating patients with surgically excised tumors with a high probability of metastasis, such as melanoma and breast cancer, by administering to such patient a nontoxic therapeutically effective amount of a 5-amino or substituted amino, 1,2,3-triazoles which are disclosed as a new class of antimetastatic agents useful in such treatment.

US PAT NO: 4,894,443 :IMAGE AVAILABLE: L4: 71 of 73
DATE ISSUED: Jan. 16, 1990
TITLE: Toxin conjugates
INVENTOR: Lawrence I. Greenfield, Albany, CA
Donald A. Kaplan, Midland, MI
Danute E. Nitecki, Berkeley, CA
ASSIGNEE: Cetus Corporation, Emeryville, CA (U.S. corp.)
APPL-NO: 06/648,759
DATE FILED: Sep. 7, 1984
ART-UNIT: 185
PRIM-EXMR: Robin L. Teskin
LEGAL-REP: Kate H. Murashige, Gregory J. Giotta, Albert P. Halluin

L4: 71 of 73
TITLE: Toxin conjugates
US PAT NO: 4,894,443 DATE ISSUED: Jan. 16, 1990
:IMAGE AVAILABLE:
APPL-NO: 06/648,759 DATE FILED: Sep. 7, 1984
REL-US-DATA: Continuation-in-part of Ser. No. 578,115, Feb. 8, 1984, abandoned.

ABSTRACT:
A novel class of polypeptides of the general formula (F-(Pro).sub.n).sub.m F, wherein F represents a flexible amino acid sequence wherein each amino acid is individually selected from the group consisting of serine, glycine, and threonine, and n is an integer from 4-8 inclusive and m is an integer from 1-4 inclusive, is disclosed. Thses polypeptides are useful in the construction of conjugates between antibodies and peptide toxins. The preparation of such conjugate toxins by linking antibodies to toxin/spacer composites prepared by recombinant techniques is also disclosed.

US PAT NO: 4,847,257 :IMAGE AVAILABLE: L4: 72 of 73
DATE ISSUED: Jul. 11, 1989
TITLE: 5-Amino or substituted amino 1,2,3,-triazoles useful as antiproliferative agents
INVENTOR: Donald Hupe, Westfield, NJ
Lawrence Argenbright, Edison, NJ
Nancy Behrens, Annandale, NJ
Barbara A. Azzolina, Denville, NJ
ASSIGNEE: Merck & Co., Inc., Rahway, NJ (U.S. corp.)
APPL-NO: 07/087,494
DATE FILED: Aug. 20, 1987
ART-UNIT: 125
PRIM-EXMR: Dale R. Ore
LEGAL-REP: Theresa Y. Cheng, Michael C. Sudol

L4: 72 of 73
TITLE: 5-Amino or substituted amino 1,2,3,-triazoles useful as antiproliferative agents
US PAT NO: 4,847,257 DATE ISSUED: Jul. 11, 1989
:IMAGE AVAILABLE:
APPL-NO: 07/087,494 DATE FILED: Aug. 20, 1987

ABSTRACT:
5-Amino or substituted amino 1,2,3-triazoles are disclosed as a new class of antiproliferative agents useful in the treating and managing of psoriasis, inflammatory bowel syndrome, cutaneous leishmanilisis and certain types of cancer.

US PAT NO: 4,837,237 :IMAGE AVAILABLE: L4: 73 of 73
DATE ISSUED: Jun. 6, 1989
TITLE: Therapy using glucosidase processing inhibitors
INVENTOR: Larry R. Rohrschneider, 1501 - 1st Ave. N., #3A, Mercer Island, WA
Everett J. Nichols, 1501 - 1st Ave. N., #3A, Seattle, WA 98109
ASSIGNEE: Fred Hutchinson Cancer Research Center, Seattle, WA (U.S. corp.)
Everett J. Nichols, Seattle, WA (U.S. indiv.)
APPL-NO: 06/753,686
DATE FILED: Jul. 9, 1985
ART-UNIT: 185
PRIM-EXMR: Blondel Hazel
LEGAL-REP: Christensen, O'Connor, Johnson & Kindness

L4: 73 of 73
TITLE: Therapy using glucosidase processing inhibitors
US PAT NO: 4,837,237 DATE ISSUED: Jun. 6, 1989
:IMAGE AVAILABLE:
APPL-NO: 06/753,686 DATE FILED: Jul. 9, 1985

ABSTRACT:
A method of regulating oncogene-mediated cell transformation in a mammalian host. Oncogenes having glycosylated expression products are regulated by administering an effective amount of a processing glucosidase inhibitor: a glucosidase I inhibitor, e.g., castanospermine, N-methyl-1-deoxynojirimycin, 1-deoxynojirimycin, 5-amino-5-deoxy-D-glucopyranose; or a glucosidase II inhibitor, e.g., bromoconduritol. The glucosidase I inhibitors are preferred, particularly castanospermine (CA) and N-methyl-1-deoxynojirimycin (MdN). Oncogenes having glycosylated expression products that are ultimately expressed on the plasma membrane or secreted from transformed cells are particularly susceptible to regulation by these anti-cancer drugs. Also provided is a method of regulating the immune system of a mammalian host. Administration of an effective amount of a processing glucosidase inhibitor suppresses proliferation and differentiation of monocytic and myeloblastic cells.

=> s lysozym? (p) (transform? or transgen?) (p) plant?
4355 LYSOZYM?
189247 TRANSFORM?
1588 TRANSGEN?

146899 PLANT?
L5 18 LYSOZYM? (P) (TRANSFORM? OR TRANSGEN?) (P) PLANT?

=> d l-18 date leg ab kwic
'D1-18' IS NOT A RECOGNIZED COMMAND

=> d 1-18 date leg ab kwic

L5: 1 of 18
TITLE: Pseudomonas syringae pv syringae hrpZ gene
US PAT NO: 5,708,139 DATE ISSUED: Jan. 13, 1998
:IMAGE AVAILABLE:
APPL-NO: 08/062,024 DATE FILED: May 17, 1993

US PAT NO: 5,708,139 :IMAGE AVAILABLE: L5: 1 of 18
DATE ISSUED: Jan. 13, 1998
TITLE: Pseudomonas syringae pv syringae hrpZ gene
INVENTOR: Alan Collmer, Ithaca, NY
Sheng-Yang He, Lexington, KY
ASSIGNEE: Cornell Research Foundation, Inc., Ithaca, NY (U.S. corp.)
APPL-NO: 08/062,024
DATE FILED: May 17, 1993
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Rebecca Prouty
LEGAL-REP: Nixon, Hargrave, Devans & Doyle

ABSTRACT:
The nucleic acid and amino acid sequences for proteinaceous elicitors of the plant defense reaction known as the hypersensitive response against Pseudomonas syringae are described along with method for preparation.

DETDESC:

DETD(27)

To circumvent the preparation of lysates ex **planta**, we developed (Example I) one aspect of the present invention, a procedure for lysing E. coli cells in **plants** through treatment with EDTA and **lysozyme** at the time of inoculation. Two out of 200 randomly chosen E. coli **transformants** (1.0%) screened by this technique were found to produce the rapid leaf tissue collapse characteristic of the HR. Collapse did. . . performed on E. coli DH5.alpha. cells lacking these two subclones. Plasmids pSYH1 and pSYH4 were isolated from the two positive **transformants**.

L5: 2 of 18
TITLE: Plant defense genes and plant defense regulatory elements
US PAT NO: 5,695,939 DATE ISSUED: Dec. 9, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/379,259 DATE FILED: Jan. 27, 1995
REL-US-DATA: Division of Ser. No. 704,288, May 22, 1991, Pat. No. 5,399,680.

US PAT NO: 5,695,939 :IMAGE AVAILABLE: L5: 2 of 18
DATE ISSUED: Dec. 9, 1997
TITLE: Plant defense genes and plant defense regulatory elements
INVENTOR: Qun Zhu, San Diego, CA
Christopher J. Lamb, San Diego, CA
ASSIGNEE: The Salk Institute for Biological Studies, La Jolla, CA (U.S. corp.)
APPL-NO: 08/379,259
DATE FILED: Jan. 27, 1995
ART-UNIT: 184
PRIM-EXMR: Eric Grimes
LEGAL-REP: Stephen E.Gray, Cary, Ware & Freidenrich Reiter

ABSTRACT:
Novel chitinase gene, and its associated regulatory region, from a monocotyledon plant is described.

DETDESC:

DETD(69)

A . . . respectively. These plasmids were transferred into Escherichia coli strain HB101 by the CaCl.sub.2 method :Maniatis et al. supra:, and the **transformed** cells grown to stationary phase at 37.degree. C. in LB broth. The cells were then inoculated into 5 ml of. . . harvested and lysed by sunication in 10 mM TRIS-HCl, pH 8.0, 50 mM EDTA, 8% sucrose, 0.5% Triton X-100, and **lysozyme** (2 mg/ml). Soluble bacterial extracts were analyzed in a 10% SDS-polyacrylamide gel :Maniatis et al. supra:. Immunoblotting was performed as described by Bradley et al., **Planta** 173: 149-160 (1988). Antiserum to bean chitinase, prepared employing standard techniques, was obtained as a gift from T. Boller.

L5: 3 of 18
TITLE: Chemically inducible promoter of a plant PR-1 gene
US PAT NO: 5,689,044 DATE ISSUED: Nov. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/449,043 DATE FILED: May 24, 1995
REL-US-DATA: Division of Ser. No. 181,271, Jan. 13, 1994, Pat. No. 5,614,395, which is a continuation-in-part of Ser. No. 93,301, Jul. 16, 1993, abandoned, which is a continuation of Ser. No. 973,197, Nov. 6, 1992, abandoned, which is a continuation of Ser. No. 678,378, Apr. 1, 1991, abandoned, which is a continuation of Ser. No. 305,566, Feb. 6, 1989, abandoned, which is a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 449,043, May 24, 1995 is a continuation-in-part of Ser. No. 42,847, Apr. 6, 1993, abandoned, which is a continuation of Ser. No. 632,441, Dec. 21, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, and a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 449,043, May 24, 1995 is a continuation-in-part of Ser. No. 848,506, Mar. 6, 1992, abandoned, which is a continuation-in-part of Ser. No. 768,122, Sep. 27, 1991, abandoned, which is a continuation-in-part of Ser. No. 568,431, Sep. 7, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 368,672, Jun. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 329,018, Mar. 24, 1989, abandoned, said Ser. No. 449,043, May 24, 1995 is a continuation-in-part of Ser. No. 45,957, Apr. 12, 1993, abandoned.

US PAT NO: 5,689,044 :IMAGE AVAILABLE: L5: 3 of 18
DATE ISSUED: Nov. 18, 1997
TITLE: Chemically inducible promoter of a plant PR-1 gene
INVENTOR: John A. Ryals, Durham, NC
Leslie B. Friedrich, Cary, NC
Scott J. Uknes, Apex, NC
Eric R. Ward, Basel, Switzerland
ASSIGNEE: Novartis Corporation, Summit, NJ (U.S. corp.)
APPL-NO: 08/449,043
DATE FILED: May 24, 1995
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: J. Timothy Meigs

ABSTRACT:
The present invention provides chemically regulatable DNA sequences capable of regulating transcription of an associated DNA sequence in plants or plant tissues, chimeric constructions containing such sequences, vectors containing such sequences and chimeric constructions, and transgenic plants and plant tissues containing these chimeric constructions. In one aspect, the chemically regulatable DNA sequences of the invention are derived from the 5' region of genes encoding pathogenisis-related (PR) proteins. The present invention also provides anti-pathogenic sequences derived from novel cDNAs coding for PR proteins which can be genetically engineered and transformed into plants to confer enhanced resistance to disease. Also provided is a method for the exogenous regulation of gene expression in plants, which comprises obtaining a plant incapable of regulating at least one gene or gene family, or at least one heterologous gene, due to the deactivation of at least one endogenous signal transduction cascade which regulates the gene in the plant, and applying a chemical regulator to the plant at a time when expression of the gene is desired. A novel signal peptide sequence and corresponding DNA coding sequence is also provided. Further provided are assays for the identification and isolation of additional chemically regulatable DNA sequences and cDNAs encoding PR proteins and assays for identifying chemicals capable of exogenously regulating the chemically regulatable DNA sequences of the invention.

SUMMARY:

BSUM(47)

Class . . . is induced by ethylene, whereas class II and class III chitinase gene expression is induced in the SAR response. The chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/329,018 and the chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/580,431 (provided herein as SEQ ID Nos. 29 and 30, respectively) are class III chitinases. It is well known that the level of chitinase activity of **plants** increases dramatically after pathogen invasion (Mauch et al., **Plant** Physiol. 76: 607-611 (1984)) and this is presumably due to the host **plant**'s attempts to degrade the chitin of the fungal cell wall. Furthermore, chitinase has been shown in vitro to inhibit fungal and insect growth, and in **transgenic** **plants** a bacterial chitinase has been shown to exhibit inhibitory effects towards numerous pathogens and pests including insects (Suslow & Jones. . .

DETDESC:

DETD(1455)

A leaf tissue sample is taken from T1 **plants** **transformed** with either of the binary vectors pCGN1779C or pCGN1779D. The cucumber chitinase/**lysozyme** protein content is determined using an ELISA assay essentially as described above except that the monoclonal and polyclonal antibodies are directed against the cucumber chitinase/**lysozyme** protein.

DETDESC:

DETD(1456)

Eight of thirteen T1 "sense" **plants** produce very high amounts (>10,000 ng/ml extract) of the cucumber chitinase foreign gene product. Again a wide range, from undetectable. . . ng/ml extract, is observed, with an average of 12,500 ng/ml extract. The conclusion from the T1 data is that the **transformed** T1 **plants** produce several thousand times more of the **transgenic** protein than is present in control **plants**. T3 seed lines are derived from the high expressing T1 **plants** as described in Example 148 and these T3 seed lines maintain their high levels of chitinase/**lysozyme** expression.

L5: 4 of 18

TITLE: Somatic embryogenesis and transformation of squash
US PAT NO: 5,677,157 DATE ISSUED: Oct. 14, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/349,759 DATE FILED: Dec. 5, 1994
REL-US-DATA: Continuation of Ser. No. 196,882, Feb. 14, 1994, abandoned, which is a continuation of Ser. No. 854,138, Mar. 18, 1992, abandoned, which is a continuation of Ser. No. 434,245, Nov. 13, 1989, abandoned, which is a continuation-in-part of Ser. No. 410,527, Sep. 20, 1989, abandoned.

US PAT NO: 5,677,157 :IMAGE AVAILABLE: L5: 4 of 18
DATE ISSUED: Oct. 14, 1997
TITLE: Somatic embryogenesis and transformation of squash
INVENTOR: Paula P. Chee, Kalamazoo, MI
ASSIGNEE: Asgrow Seed Company (U.S. corp.)
APPL-NO: 08/349,759
DATE FILED: Dec. 5, 1994
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Fitzpatrick, Cella, Harper & Scinto

ABSTRACT:
A method involving somatic embryogenesis of various squash (Cucurbita pepo L.) tissues is described which can be used for the regeneration of normal squash plants. This method is also used for the transfer and integration of genetic materials into the genome of squash plants, which belong to the family Cucurbitaceae, followed by regeneration of such transformed plants. Thus regenerated transformed whole squash plants are produced by this method.

DETDESC:

DETD(42)

This example is to illustrate how to generate **plant** expressible genes which allow a **plant** to be resistant to infections by bacteria and fungi. In nature, several classes of polypeptides have been isolated and found to convey broad-spectrum antimicrobial activity; for example, magainins (Zasloff, 1987), defensins (Daher et al., 1988), **lysozymes** (Boman et al., 1985), Cecropins (Boman et al., 1989), attacins (Haltmark et al., 1983), thionins (Bohlmann et al., 1988), and. . . like. Genes encoding these antimicrobial peptides or their more active modified forms can be synthesized and engineered for expression in **plants**. Promoters for the expression of these antimicrobial polypeptide genes can include the constitutive type or others which have tissue specificity.. . . attack by bacterial or fungi, or both pests. Thus the engineering of genes encoding antimicrobial polypeptide genes combined with the **plant** **transformation** and regeneration schemes described in the embodiment and Examples 1 and 2 would allow for the transfer of a useful trait to squash **plants**. Chart 5 summarizes the construction of plasmids which could be used with the Agrobacterium-mediated and microprojectile-mediated gene transfer systems.

L5: 5 of 18

TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
US PAT NO: 5,670,349 DATE ISSUED: Sep. 23, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/282,581 DATE FILED: Jul. 29, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 100,816, Aug. 2, 1993, abandoned.

US PAT NO: 5,670,349 :IMAGE AVAILABLE: L5: 5 of 18
DATE ISSUED: Sep. 23, 1997
TITLE: HMG2 promoter expression system and post-harvest production of gene products in plants and plant cell cultures
INVENTOR: Carole Lyn Cramer, Blacksburg, VA
Deborah Louise Weissenborn, Blacksburg, VA
ASSIGNEE: Virginia Tech Intellectual Properties, Inc., Blacksburg, VA (U.S. corp.)
APPL-NO: 08/282,581
DATE FILED: Jul. 29, 1994
ART-UNIT: 183
PRIM-EXMR: Elizabeth McElwain
LEGAL-REP: Pennie & Edmonds LLP

ABSTRACT:
The invention relates in part to plant HMG2 HMGR genes and in part to the "post-harvest" production method of producing gene product of interest in plant tissues and cultures. The HMG2 promoter elements are responsive to pathogen-infection, pest-infestation, wounding, or elicitor or chemical treatments. The HMG2 elements are also active in specialized tissues of the plant including pollen and mature fruits. HMG2 promoter elements and HMG2-derived promoters can be advantageously used to drive the expression of disease and pest resistance genes, whereby transgenic plants having such gene constructs would be resistant to the targeted disease and pest. In particular, the HMG2 gene expression system can be utilized in developing nematode resistant plants. The post-harvest production method of the invention utilizes plant tissues and cell cultures of plants or plant cells engineered with a expression construct comprising an inducible promoter, such as the HMG2 promoter, operably linked to a gene of interest. Production of the desired gene product is obtained by harvesting, followed by inducing and processing the harvested tissue or culture. The post-harvest production method may be advantageously used to produce direct or indirect gene products that are labile, volatile, toxic, hazardous, etc.

DETDESC:

DETD(11)

TABLE 3

Inducible **Plant** Genes with Potential for Post-harvest Induction and Accumulation of
Transgene Products. An asterisk designates those genes for which promoters have been isolated
and characterized. References represent one to two representative. . .
Tobacco, bean,
tomato
Class I and II chitinase, acidic
Extracellular, antifungal
Bean
Class II chitinase Bifunctional **lysozyme**,
Cucumber, tobacco,
chitinase barley, peturia
*.beta.-1,3-Glucanase.sup.21
Antifungal, chitinase
Bean, tobacco,
potato,
synergist pea, rice,. . . 1989, EMBO J. 8:1641-1648.
.sup.3 BeckerAndre et al., 1991, J. Biol. Chem. 266:8551-8559.
.sup.4 Arias et al., 1993, **Plant** Cell 5:485-496.
.sup.5 Doerner et al., 1990, Bio/Technology 8:845-848.
.sup.6 Mehdy et al., 1987, EMBO J. 6:1527-1533.
.sup.7 Hain et al., 1993, Nature 361:153-156.
.sup.8 Paiva et al., 1991, **Plant** Mol. Biol. 17:653-667.
.sup.9 Park et al., 1992, **Plant** Mol. Biol. 20:327-331.
.sup.10 Yang et al., 1991, **Plant** Cell 3:397-405.
.sup.11 Lois et al., 1990, Arch. Biochem. Biophys. 276:270-277.
.sup.12 Schuch et al., 1991, 3rd Int. Cong. **Plant** Mol. Biol., Tucson, Az. Abstract 1653.
.sup.13 Jaeck et al., 1992, Mol. **PlantMicrobe** Interact. 5:294-300.
.sup.14 Lagrimini et al., 1987, Proc. Natl. Acad. Sci. USA 84:7542-7546.
.sup.15 Showalter et al., 1992, **Plant** Mol. Biol. 19:205-215.
.sup.16 Wycoff et al., 1992, in D. P. S. Verma, ed., Molecular Signals in **PlantMicrobe** Communication, Boca Raton, FL: CRC Press. pgs. 407-422.
.sup.17 Bohlmann et al., 1988, EMBO J. 7:1559-1565.
.sup.18 Hedrick et al., 1988, **Plant** Physiol. 86:182-186.
.sup.19 Roby et al., 1990, **Plant** Cell 2:999-1007.
.sup.20 Sarnac and Shah, 1991, **Plant** Cell 3:1063-1072.
.sup.21 Legrand et al., 1987, Proc. Natl. Acad. Sci. USA 84:6750-6754.
.sup.22 Benhamou et al., 1991, **Plant** Physiol. 97:739-750.
.sup.23 Ryan, C. A., 1990, Annu. Rev. Phytopathol. 28:425-449.
.sup.24 Keil et al., 1989, EMBO J. 8:1323-1330.

.sup.25 Bowler et al., 1989, EMBO J. 8:31-38.
.sup.26 Melan et al., 1993, **Plant** Physiol. 101:441-450.
.sup.27 Cornelissen et al., 1986, EMBO J. 5:37-40.
.sup.28 Meler et al., 1991, **Plant** Cell 3:309-315.
.sup.29 Sharma et al., 1992, Mol. **PlantMicrobe** Interact. 5:89-95.
.sup.30 Cornelissen et al., 1986, Nature 321:531-532.
.sup.31 Stinizi et al., 1991, Physiol. Mol. **Plant** Pathol. 38:137-146.
.sup.32 Kononowicz et al., 1992, **Plant** Cell 4:513-524.
.sup.33 Rickey and Belknap, 1991, **Plant** Mol. Biol. 16:1009-1018.
.sup.34 Weiss and Bevan, 1991, **Plant** Physiol. 96:943-951.
.sup.35 Logemann et al., 1988, Proc. Natl. Acad. Sci. USA 85:1136-1140.
.sup.36 An et al., 1990, **Plant** Cell 2:225-233.
.sup.37 Li et al., 1992, **Plant** Mol. Biol. 18:477-487.
.sup.38 Chol et al., 1992, **Plant** Cell 4:1333-1344.
.sup.39 Dyer et al., 1989, Proc. Natl. Acad. Sci. USA 86:7370-7373.
.sup.40 Ward et al., 1991, **Plant** Cell 3:1085-1094.
.sup.41 Van de Rhee et al., 1990, **Plant** Cell 2:357-366.
.sup.42 Mason et al., 1993, **Plant** Cell 5:241-251.
.sup.43 Ho and Sachs, 1989, In: Stump.sub.-- and Conn, eds., The Biochemistry of **Plants**: A Comprehensive Treatis, Vol. 15, pgs. 347-377.
.sup.44 Thomashow, 1992, In: Scandalios and Wright, eds., Genomic Responses to Environmental Stress, Adv. in Genetics, Vol. 28, pgs. 99-131
.sup.45 Skriver and Mundy, 1990, **Plant** Cell 2:503-512.
.sup.46 Gubler and Jacobsen, 1992, **Plant** Cell 4:1435-1441.
.sup.47 Chandler and Robertson, 1994, Annu. Rev. **Plant** Physiol. **Plant** Mol Biol. 45:113-142.

L5: 6 of 18

TITLE: Chemically inducible promoter of a cucumber chitinase/lysozyme gene
US PAT NO: 5,654,414 DATE ISSUED: Aug. 5, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/444,803 DATE FILED: May 19, 1995
REL-US-DATA: Division of Ser. No. 181,271, Jan. 13, 1994, Pat. No. 5,614,395, which is a continuation-in-part of Ser. No. 93,301, Jul. 16, 1993, abandoned, which is a continuation of Ser. No. 973,197, Nov. 6, 1992, abandoned, which is a continuation of Ser. No. 678,378, Apr. 1, 1991, abandoned, which is a continuation of Ser. No. 305,566, Feb. 6, 1989, abandoned, which is a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 444,803, May 19, 1995 is a continuation-in-part of Ser. No. 42,847, Apr. 6, 1993, abandoned, which is a continuation of Ser. No. 632,441, Dec. 21, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, and a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 444,803, May 19, 1995 is a continuation-in-part of Ser. No. 848,506, Mar. 6, 1992, abandoned, which is a continuation-in-part of Ser. No. 768,122, Sep. 27, 1991, abandoned, which is a continuation-in-part of Ser. No. 580,431, Sep. 7, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 368,672, Jun. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 329,018, Mar. 24, 1989, abandoned, said Ser. No. 444,803, May 19, 1995 is a continuation-in-part of Ser. No. 45,957, Apr. 12, 1993, abandoned.

US PAT NO: 5,654,414 :IMAGE AVAILABLE: L5: 6 of 18
DATE ISSUED: Aug. 5, 1997
TITLE: Chemically inducible promoter of a cucumber chitinase/lysozyme gene
INVENTOR: John A. Ryals, Cary, NC
James J. Beck, Apex, NC
Leslie B. Friedrich, Cary, NC
ASSIGNEE: Novartis Finance Corporation, New York, NY (U.S. corp.)
APPL-NO: 08/444,803
DATE FILED: May 19, 1995
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: J. Timothy Meigs

ABSTRACT:
The present invention provides chemically regulatable DNA sequences capable of regulating transcription of an associated DNA sequence in plants or plant tissues, chimeric constructions containing such sequences, vectors containing such sequences and chimeric constructions, and transgenic plants and plant tissues containing these chimeric constructions. In one aspect, the chemically regulatable DNA sequences of the invention are derived from the 5' region of genes encoding pathogenisis-related (PR) proteins. The present invention also provides anti-pathogenic sequences derived from novel cDNAs coding for PR proteins which can be genetically engineered and transformed into plants to confer enhanced resistance to disease. Also provided is a method for the exogenous regulation of gene expression in plants, which comprises obtaining a plant incapable of regulating at least one gene or gene family, or at least one heterologous gene, due to the deactivation of at least one endogenous signal transduction cascade which regulates the gene in the plant, and applying a chemical regulator to the plant at a time when expression of the gene is desired. A novel signal peptide sequence and corresponding DNA coding sequence is also provided. Further provided are assays for the identification and isolation of additional chemically regulatable DNA sequences and cDNAs encoding PR proteins and assays for identifying chemicals capable of exogenously regulating the chemically regulatable DNA sequences of the invention.

SUMMARY:

BSUM(47)

Class . . . is induced by ethylene, whereas class II and class III chitinase gene expression is induced in the SAR response. The chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/329,018 and the chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/580,431 (provided herein as SEQ ID Nos. 29 and 30, respectively) are class III chitinases. It is well known that the level of chitinase activity of **plants** increases dramatically after pathogen invasion (Mauch et al., **Plant** Physiol. 76: 607-611 (1984)) and this is presumably due to the host **plant**'s attempts to degrade the chitin of the fungal cell wall. Furthermore, chitinase has been shown in vitro to inhibit fungal and insect growth, and in **transgenic** **plants** a bacterial chitinase has been shown to exhibit inhibitory effects towards numerous pathogens and pests including insects (Suslow & Jones. . .

DETDESC:

DETD(1449)

A leaf tissue sample is taken from T1 **plants** **transformed** with either of the binary vectors pCGN1779C or pCGN1779D. The cucumber chitinase/**lysozyme** protein content is determined using an ELISA assay essentially as described above except that the monoclonal and polyclonal antibodies are directed against the cucumber chitinase/**lysozyme** protein.

DETDESC:

DETD(1450)

Eight of thirteen T1 "sense" **plants** produce very high amounts (>10,000 ng/ml extract) of the cucumber chitinase foreign gene product Again a wide range, from undetectable. . . ng/ml extract, is observed, with an average of 12,500 ng/ml extract. The conclusion from the T1 data is that the **transformed** T1 **plants** produce several thousand times more of the **transgenic** protein than is present in control **plants**. T3 seed lines are derived from the high expressing T1 **plants** as described in Example 148 and these T3 seed lines maintain their high levels of chitinase/**lysozyme** expression.

L5: 7 of 18

TITLE: Chemically regulatable and anti-pathogenic DNA sequences and uses thereof
US PAT NO: 5,650,505 DATE ISSUED: Jul. 22, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/449,315 DATE FILED: May 24, 1995
REL-US-DATA: Division of Ser. No. 181,271, Jan. 13, 1994, Pat. No. 5,614,395, and a continuation-in-part of Ser. No. 42,847, Apr. 6, 1993, abandoned, Ser. No. 848,506, Mar. 6, 1992, abandoned, and Ser. No. 45,957, Apr. 12, 1993, abandoned, said Ser. No. 181,271 is a continuation-in-part of Ser. No. 93,301, Jul. 16, 1993, abandoned, which is a continuation of Ser. No. 973,197, Nov. 6, 1992, abandoned, which is a continuation of Ser. No. 678,378, Apr. 1, 1991, abandoned, which is a continuation of Ser. No. 305,566, Feb. 6, 1989, abandoned, which is a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 42,847 is a continuation of Ser. No. 632,441, Dec. 21, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, and Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 848,506 is a continuation-in-part of Ser. No. 768,122, Sep. 27, 1991, abandoned, which is a continuation-in-part of Ser. No. 580,431, Sep. 7, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 368,672, Jun. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 329,018, Mar. 24, 1989, abandoned.

US PAT NO: 5,650,505 :IMAGE AVAILABLE: L5: 7 of 18

DATE ISSUED: Jul. 22, 1997
TITLE: Chemically regulatable and anti-pathogenic DNA sequences and uses thereof
INVENTOR: John A. Ryals, Durham, NC
Danny C. Alexander, Cary, NC
James J. Beck, Cary, NC
John H. Duesing, Riehen, Switzerland
Robert M. Goodman, Madison, WI
Leslie B. Friedrich, Cary, NC
Christian Harms, Bad Krozingen, Federal Republic of Germany
Frederich Meins, Jr., Reihen, Switzerland
Alice Montoya, deceased, late of Lake Stevens, WA, by Terry Montoya, legal representative
Mary B. Moyer, Cary, NC
Jean-Marc Neuhaus, Basel, Switzerland
George B. Payne, Ann Arbor, MI
Christoph Sperisen, Dulliken, Switzerland
Jeffrey R. Stinson, Davie, FL
Scott J. Uknes, Apex, NC
Eric R. Ward, Basel, Switzerland
Shericca C. Williams, Cary, NC
ASSIGNEE: Novartis Corporation, Tarrytown, NY (U.S. corp.)
APPL-NO: 08/449,315
DATE FILED: May 24, 1995
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody
LEGAL-REP: J. Timothy Meigs

ABSTRACT:
The present invention provides chemically regulatable DNA sequences capable of regulating transcription of an associated DNA sequence in plants or plant tissues, chimeric constructions containing such sequences, vectors containing such sequences and chimeric constructions, and transgenic plants and plant tissues containing these chimeric constructions. In one aspect, the chemically regulatable DNA sequences of the invention are derived from the 5' region of genes encoding pathogenisis-related (PR) proteins. The present invention also provides anti-pathogenic sequences derived from novel cDNAs coding for PR proteins which can be genetically engineered and transformed into plants to confer enhanced resistance to disease. Also provided is a method for the exogenous regulation of gene expression in plants, which comprises obtaining a plant incapable of regulating at least one gene or gene family, or at least one heterologous gene, due to the deactivation of at least one endogenous signal transduction cascade which regulates the gene in the plant, and applying a chemical regulator to the plant at a time when expression of the gene is desired. A novel signal peptide sequence and corresponding DNA coding sequence is also provided. Further provided are assays for the identification and isolation of additional chemically regulatable DNA sequences and cDNAs encoding PR proteins and assays for identifying chemicals capable of exogenously regulating the chemically regulatable DNA sequences of the invention.

SUMMARY:

BSUM(47)

Class . . . is induced by ethylene, whereas class II and class III chitinase gene expression is induced in the SAR response. The chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/329,018 and the chitinase/**lysozyme** disclosed in U.S. Application Ser. No. 07/580,431 (provided herein as SEQ ID Nos. 29 and 30, respectively) are class III chitinases. It is well known that the level of chitinase activity of **plants** increases dramatically after pathogen invasion (Mauch et al., **Plant** Physiol. 76: 607-611 (1984)) and this is presumably due to the host **plant**'s attempts to degrade the chitin of the fungal cell wall. Furthermore, chitinase has been shown in vitro to inhibit fungal and insect growth, and in **transgenic** **plants** a bacterial chitinase has been shown to exhibit inhibitory effects towards numerous pathogens and pests including insects (Suslow & Jones. . .

DETDESC:

DETD(1419)

A leaf tissue sample is taken from T1 **plants** **transformed** with either of the binary vectors pCGN 1779C or pCGN1779D. The cucumber chitinase/**lysozyme** protein content is determined using an ELISA assay essentially as described above except that the monoclonal and polyclonal antibodies are directed against the cucumber chitinase/**lysozyme** protein.

DETDESC:

DETD(1420)

Eight of thirteen T1 "sense" **plants** produce very high amounts (>10,000 ng/ml extract) of the cucumber chitinase foreign gene product. Again a wide range, from undetectable. . . ng/ml extract, is observed, with an average of 12,500 ng/ml extract. The conclusion from the T1 data is that the **transformed** T1 **plants** produce several thousand times more of the **transgenic** protein than is present in control **plants**. T3 seed lines are derived from the high expressing T1 **plants** as described in Example 148 and these T3 seed lines maintain their high levels of chitinase/**lysozyme** expression.

L5: 8 of 18
TITLE: Plant promoter useful for directing the expression of foreign proteins to the plant epidermis
US PAT NO: 5,646,333 DATE ISSUED: Jul. 8, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/299,953 DATE FILED: Sep. 2, 1994

US PAT NO: 5,646,333 :IMAGE AVAILABLE: L5: 8 of 18
DATE ISSUED: Jul. 8, 1997
TITLE: Plant promoter useful for directing the expression of foreign proteins to the plant epidermis
INVENTOR: Michael S. Dobres, Philadelphia, PA
Sevnur Mandaci, Ardsley, PA
ASSIGNEE: Drexel University, Philadelphia, PA (U.S. corp.)
APPL-NO: 08/299,953
DATE FILED: Sep. 2, 1994
ART-UNIT: 183
PRIM-EXMR: Douglas W. Robinson
ASST-EXMR: Elizabeth F. McElwain
LEGAL-REP: Woodcock Washburn Kurtz Mackiewicz & Norris

ABSTRACT:
The present invention is directed to a Blec plant promoter sequence of SEQUENCE ID NO: 1. A method of transforming plants with a Blec promoter--gene construct is also within the scope of the present invention. The present invention is also directed to cells comprising a Blec promoter--gene construct, plasmids and vectors comprising a Blec promoter--gene construct and the constructs per se comprising a Blec promoter and a gene. A plant extract comprising all or part of the Blec promoter sequence and a gene under control of said promoter and a method of transcribing nucleic acids comprising an extract having all or part of the Blec promoter sequence and a gene under control of said promoter are also within the scope of the present invention.

DETDESC:

DETD(19)

The present invention includes the **transformation** of **plants** with genes which provide advantageous characteristics, including and not limited to altering (increasing or decreasing) insect, viral, and/or disease resistance;. . . proteins induced by wounding or microbial attack, including those induced by salicylic acid, jasmonic acid, 2, 6, 1, chloroisonicotinic acid; **lysozymes** from non-**plant** sources including and not limited to phage T4 **lysozyme**, mammalian **lysozymes**; phenylammonia lyase or other enzymes of the phenylpropanoid pathway which catalyze the formation of a wide range of natural products. . . as cowpea trypsin inhibitor; cell wall proteins including glycine hydroxyproline rich proteins such as extensins; enzymes involved in cellulose biosynthesis, **plant** cuticle biosynthesis including lipid biosynthesis and transport; RNases and ribozymes; and the like.

L5: 9 of 18
TITLE: Chemically regulatable and anti-pathogenic DNA sequences and uses thereof
US PAT NO: 5,614,395 DATE ISSUED: Mar. 25, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/181,271 DATE FILED: Jan. 13, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 93,301, Jul. 16, 1993, abandoned, Ser. No. 42,847, Apr. 6, 1993, abandoned, Ser. No. 45,957, Apr. 12, 1993, abandoned, and Ser. No. 848,506, Mar. 6, 1992, abandoned, which is a continuation-in-part of Ser. No. 768,122, Sep. 27, 1991, abandoned, which is a continuation-in-part of Ser. No. 580,431, Sep. 7, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 368,672, Jun. 20, 1989, abandoned, which is a continuation-in-part of Ser. No. 329,018, Mar. 24, 1989, abandoned, said Ser. No. 93,301 is a continuation of Ser. No. 973,197, Nov. 6, 1992, abandoned, which is a continuation of Ser. No. 678,378, Apr. 1, 1991, abandoned, which is a continuation of Ser. No. 305,566, Feb. 6, 1989, abandoned, which is a continuation-in-part of Ser. No. 165,667, Mar. 8, 1988, abandoned, said Ser. No. 42,847 is a continuation of Ser. No. 632,441, Dec. 21, 1990, abandoned, which is a continuation-in-part of Ser. No. 425,504, Oct. 20, 1989, abandoned, and Ser. No. 165,667, Mar. 8, 1988, abandoned.

US PAT NO: 5,614,395 :IMAGE AVAILABLE: L5: 9 of 18

DATE ISSUED: Mar. 25, 1997
TITLE: Chemically regulatable and anti-pathogenic DNA sequences and uses thereof
INVENTOR: John A. Ryals, Durham, NC
Danny C. Alexander, Cary, NC
James J. Beck, Cary, NC
John H. Duesing, Riehen, Switzerland
Robert M. Goodman, Madison, WI
Leslie B. Friedrich, Cary, NC
Christian Harms, Bad Krozingen, Federal Republic of Germany
Frederich Meins, Jr., Reihen, Switzerland
Alice Montoya, deceased, late of Lake Stevens, WA, by Terry Montoya, legal representative
Mary B. Moyer, Cary, NC
Jean-Marc Neuhaus, Basel, Switzerland
George B. Payne, Ann Arbor, MI
Christoph Sperisen, Dulliken, Switzerland
Jeffrey R. Stinson, Davie, FL
Scott J. Uknes, Apex, NC
Eric R. Ward, Basel, Switzerland
Shericca C. Williams, Cary, NC
ASSIGNEE: Ciba-Geigy Corporation, Tarrytown, NY (U.S. corp.)
APPL-NO: 08/181,271
DATE FILED: Jan. 13, 1994
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody
LEGAL-REP: J. Timothy Meigs, Andrea C. Walsh

ABSTRACT:
The present invention provides chemically regulatable DNA sequences capable of regulating transcription of an associated DNA sequence in plants or plant tissues, chimeric constructions containing such sequences, vectors containing such sequences and chimeric constructions, and transgenic plants and plant tissues containing these chimeric constructions. In one aspect, the chemically regulatable DNA sequences of the invention are derived from the 5' region of genes encoding pathogenisis-related (PR) proteins. The present invention also provides anti-pathogenic sequences derived from novel cDNAs coding for PR proteins which can be genetically engineered and transformed into plants to confer enhanced resistance to disease. Also provided is a method for the exogenous regulation of gene expression in plants, which comprises obtaining a plant incapable of regulating at least one gene or gene family, or; at least one heterologous gene, due to the deactivation of at least one endogenous signal transduction cascade which regulates the gene in the plant, and applying a chemical regulator to the plant at a time when expression of the gene is desired. A novel signal peptide sequence and corresponding DNA coding sequence is also provided. Further provided are assays for the identification and isolation of additional chemically regulatable DNA sequences and cDNAs encoding PR proteins and assays for identifying chemicals capable of exogenously regulating the chemically regulatable DNA sequences of the invention.

SUMMARY:

BSUM(47)

Class . . . is induced by ethylene, whereas class II and class III chitinase gene expression is induced in the SAR response. The chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/329,018 and the chitinase/**lysozyme** disclosed in U.S. application Ser. No. 07/580,431 (provided herein as SEQ ID Nos. 29 and 30, respectively) are class III chitinases. It is well known that the level of chitinase activity of **plants** increases dramatically after pathogen invasion (Mauch et al., **Plant** Physiol. 76: 607-611 (1984)) and this is presumably due to the host planes attempts to degrade the chitin of the fungal cell wall. Furthermore, chitinase has been shown in vitro to inhibit fungal and insect growth, and in **transgenic** **plants** a bacterial chitinase has been shown to exhibit inhibitory effects towards numerous pathogens and pests including insects (Suslow & Jones. . .

DETDESC:

DETD(1576)

A leaf tissue sample is taken from T1 **plants** **transformed** with either of the binary vectors pCGN1779C or pCGN1779D. The cucumber chitinase/**lysozyme** protein content is determined using an ELISA assay essentially as described above except that the monoclonal and polyclonal antibodies are directed against the cucumber chitinase/**lysozyme** protein.

DETDESC:

DETD(1577)

Eight of thirteen T1 "sense" **plants** produce very high amounts (>10,000 ng/ml extract) of the cucumber chitinase foreign gene product. Again a wide range, from undetectable. . . ng/ml extract, is observed, with an avenge of 12,500 ng/ml extract. The conclusion from the T1 dam is that the **transformed** T1 **plants** produce several thousand times more of the **transgenic** protein than is present in control **plants**. T3 seed lines are derived from the high expressing T1 **plants** as described in Example 148 and these T3 seed lines maintain their high levels of chitinase/**lysozyme** expression.

L5: 10 of 18

TITLE: Plants genetically enhanced for disease resistance
US PAT NO: 5,597,945 DATE ISSUED: Jan. 28, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/453,436 DATE FILED: May 30, 1995
REL-US-DATA: Continuation of Ser. No. 152,933, Nov. 15, 1993, abandoned, which is a continuation of Ser. No. 994,085, Dec. 16, 1992, abandoned, which is a continuation of Ser. No. 817,950, Jan. 3, 1992, abandoned, which is a continuation of Ser. No. 646,449, Jan. 25, 1991, abandoned, which is a continuation of Ser. No. 115,941, Nov. 2, 1987, abandoned, which is a continuation-in-part of Ser. No. 889,225, Jul. 25, 1986, abandoned.

US PAT NO: 5,597,945 :IMAGE AVAILABLE: L5: 10 of 18
DATE ISSUED: Jan. 28, 1997
TITLE: Plants genetically enhanced for disease resistance
INVENTOR: Jesse M. Jaynes, Baton Rouge, LA
Kenneth S. Derrick, Lake Alfred, FL
ASSIGNEE: Board of Supervisors of Louisiana State University and Agricultural and Mechanical College, Baton Rouge, LA (U.S. corp.)
APPL-NO: 08/453,436
DATE FILED: May 30, 1995
ART-UNIT: 183
PRIM-EXMR: David T. Fox

ABSTRACT:
Plant **transformants** having an expressible heterologous gene for an antimicrobial agent for disease resistance and/or a protein high in limiting essential amino acid content for enhanced nutritional quality. Monocots, dicots and gymnosperms are genetically enhanced for disease resistance to express a lytic peptide such as cecropin, attacin or **lysozyme**, or an antiviral antisense micRNA. The nutritional quality of **plants** cultivated for food is enhanced by a gene expressing a protein containing 25-60 weight percent of methionine, lysine, tryptophan, threonine and isoleucine. Methods for obtaining such **transformants**, novel expressing vectors, novel proteins high in essential amino acids, and novel lytic peptides are also disclosed.

ABSTRACT:
Plant **transformants** having an expressible heterologous gene for an antimicrobial agent for disease resistance and/or a protein high in limiting essential amino. . . Monocots, dicots and gymnosperms are genetically enhanced for disease resistance to express a lytic peptide such as cecropin, attacin or **lysozyme**, or an antiviral antisense micRNA. The nutritional quality of **plants** cultivated for food is enhanced by a gene expressing a protein containing 25-60 weight percent of methionine, lysine, tryptophan, threonine and isoleucine. Methods for obtaining such **transformants**, novel expressing vectors, novel proteins high in essential amino acids, and novel lytic peptides are also disclosed.

DETDESC:

DETD(91)

The P22 **lysozyme** is then rescued from pMONP22Ly and inserted into pBI121 which is then used to **transform** E. coli, which in turn is conjugated with A. tumefaciens and used to infect tobacco leaf discs as described in Example 1. Callus eventually develops, and **plants** regenerated therefrom express the phage **lysozyme** gene and are resistant to P. syringae.

DETDESC:

DETD(100)
was . . . fragment after digestion with enzyme XmnI. Then the fragment was digested with SalI and cloned into the plasmid pBR322. The **lysozyme** gene was rescued by digestion with enzyme Bgl II and inserted into the **plant** vector pMON237. The plasmid pMON237 is similar to pMON530 except that it has the 19s promoter instead of the 35s,. . . the BglII and EcoR1 restriction sites near bp O. The procedure of Example 1 is then followed to place the **lysozyme** gene in pCAMV2X and to obtain **plant** **transformants**.

DETDESC:

DETD(135)

The . . . essential amino acid content. First, potato leaf discs are used instead of tobacco according to the procedure of Example 1. **Transformants** obtained thereby are then treated with a pCAMV2X vector

similar to that of Example 2 except that a different antibiotic resistance marker is present in the plasmid construct for selection of **transformants**. **Transformants** expressing the antimicrobial genes of Examples 1 and 2 are then sequentially **transformed** in the same manner with the vectors of Examples 3-9 and 13, using a different selectable marker in each **transformation** stage. The resulting potato **plants** express attacin, **lysozyme**, cecropin, and the protein of Example 13, and have resistance to a wide spectrum of bacteria, fungi and viruses, as. . .

L5: 11 of 18

TITLE: Use of lysozyme gene structures in plants to increase resistance
US PAT NO: 5,589,626 DATE ISSUED: Dec. 31, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/389,085 DATE FILED: Feb. 14, 1995
FRN-PR. NO: 39 26 390.8 FRN FILED: Aug. 10, 1989
FRN-PR. CO: Federal Republic of Germany
REL-US-DATA: Continuation of Ser. No. 163,493, Dec. 7, 1993, abandoned, which is a division of Ser. No. 555,557, Jul. 19, 1990, Pat. No. 5,349,122, Sep. 20, 1994.

US PAT NO: 5,589,626 :IMAGE AVAILABLE: L5: 11 of 18
DATE ISSUED: Dec. 31, 1996
TITLE: Use of lysozyme gene structures in plants to increase resistance
INVENTOR: Rudiger Hain, Langenfeld, Federal Republic of Germany
Klaus Stenzel, Duesseldorf, Federal Republic of Germany
ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/389,085
DATE FILED: Feb. 14, 1995
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Sprung Horn Kramer & Woods

ABSTRACT:
A method for increasing the resistance of a plant to fungi and animal pests comprising introducing into the genome of the plant one or more lysozyme gene structures which express lysozyme, the lysozyme gene structure comprises a chimeric gene fusion of the TR promoter, the signal peptide sequence of barley alpha-amylase and one or more lysozyme genes.

SUMMARY:

BSUM(4)

Patent application WO 89/04371 describes the **transformation** of **plants** having specific **lysozyme** genes for increasing the resistance to specific bacteria.

SUMMARY:

BSUM(61)

Transformed **plant** cells (including protoplasts) and **plants** (including seeds and parts of **plants**) which have an increased resistance to fungi and animal pests and which contain one or more of the **lysozyme** gene structures, as well as those **transformed** **plant** cells and **plants** which can be obtained by the above method, are also a subject of the present invention.

SUMMARY:

BSUM(63)
(a) use of **lysozyme** gene structures which consist of chimeric gene fusions of the TR promoter, the signal peptide sequence of barley alpha-amylase and one or more **lysozyme** genes or contain these chimeric gene fusions and the use of vectors and of **transformed** microorganisms according to the invention which contain the **lysozyme** gene structure, for **transforming** **plant** cells (including protoplasts) and **plants** (including seeds and parts of **plants**) with the result of an increased resistance to fungi and animal pests, as well as the

SUMMARY:

BSUM(72)

For. . . derivatives thereof (Zambryski et al. 1983), with customary methods (for example, Van Haute et al. 1983). The success of the **transformation** can be checked by detecting nopalin or NPT(II). Alternatively, the **lysozyme** gene structure can be cloned in a binary vector (for example, Koncz and Schell 1986) and transferred as described above to a suitable Agrobacterium strain (Koncz and Schell 1986). The resulting Agrobacterium strain, which contains the **lysozyme** gene structure into a form which can be transferred into **plants**, is used further for **transforming** **plants**.

SUMMARY:

BSUM(75)

Transformed (**transgenic**) **plants**, or **plant** cells, are prepared by known methods, for example by leaf-disc **transformation** (for example Horsch et al. 1985), by coculturing regenerating **plant** protoplasts or cell cultures with Agrobacterium tumefaciens (for example Marton et al. 1979, Hain et al. 1985), or by direct DNA-transfection. Resulting **transformed** **plants** are detected either by selection for reporter gene expression, for example, by phosphorylation of kanamycin sulphate in vitro (Reis et. . . 1984; Schreier et al. 1985), or by the expression of nopalin synthase (according to Aerts et al. 1983) or of **lysozyme** by Northern-blot analysis and Western blot analysis. It is also possible to detect the **lysozyme** in **transformed** **plants** in a known manner using specific antibodies.

SUMMARY:

BSUM(77)

The **transformed** **plant** cell as well as the **transformed** **plants** which contain **lysozymes**, show a considerably better resistance to phytopathogenic fungi and animal pests, in particular to insects, mites and nematodes.

DETDESC:

DETD(57)

In the **plant** cells and **plants** obtained according to the above examples, the presence of the **lysozyme** gene was confirmed by Southern blot analysis. The expression of the **lysozyme** gene was detected by Northern blot analysis and **lysozyme** with the aid of specific antibodies. **Transformed** and non-**transformed** **plants** (for comparison) were sprayed with a spore suspension of Botrytis cinera and Alternaria longipes, and infestation with the fungus was scored 1 week later. Compared with the non-**transformed** comparison **plants**, the **transformed** **plants** showed an increased resistance to infestation with fungus.

DETDESC:

DETD(63)

TABLE I

Effect of the **lysozyme** gene on the infestation of the tobacco **plants** with Alternaria longipes

	% infested leaf area on leaf					
Plant	1	2	3	4	x	Reduction*
SR.sub.1 wild type	40	43	35	33	38	--
Transformed **plant**	14	11	2	2	7	82%

*)Reduction calculated with Abbott's formula

DETDESC:

DETD(64)

TABLE II

Effect of the **lysozyme** gene on the infestation of the tobacco **plants** with Botrytis cinerea

	% infested leaf area on leaf					
Plant	1	2	3	4	x	Reduction
SR.sub.1 wild type	100	100	100	100	100	--
Transformed **plant**	23	35	23	30	28	72%

*)Reduction calculated by Abbott's formula

DETDESC:

DETD(78)

The following literature references can be cited in connection with the **transformation** of **plants** or **plant** cells and with **lysozyme** genes which can be used according to the invention:

CLAIMS:

CLMS(1)

What is claimed is:

1. A method for **transforming** a **plant** to confer on the **transformed** **plant** an increased resistance to a fungus, wherein said **plant** is other than a solanaceous **plant**, said method comprising introducing into the genome of the **plant** one or more **lysozyme** gene structures and then assaying the **plant** for increased resistance to said fungus, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimeric gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase and one or more **lysozyme** genes, and said **transformed** **plant**, as a result of being **transformed** with said **lysozyme** gene structures, exhibiting an increased resistance to said fungus as compared to a **plant** of the same species which is not so **transformed**.

CLAIMS:

CLMS(5)

5. **Transformed** **plant** cells, said **transformed** **plant** cells being of a **plant** other than a solanaceous **plant**, said **transformed** **plant** cells comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimeric gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase and one or more **lysozyme** genes, and said **transformed** **plant** cells, as a result of being **transformed** with said **lysozyme** gene structures, exhibiting an increased resistance to said fungus as compared to a **plant** cell of the same **plant** species and cell type which is not so **transformed**.

CLAIMS:

CLMS(7)

7. **Transformed** **plant** cells according to claim 5 wherein the **lysozyme** gene is of non-**plant** origin.

CLAIMS:

CLMS(8)

8. **Transformed** **plant** cells according to claim 5 wherein the **lysozyme** gene is selected from a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene and combinations thereof.

CLAIMS:

CLMS(9)

9. **Transformed** **plant** cells according to claim 5 wherein the **lysozyme** gene structure a) is contained on plasmid pSR 2-4 or b) is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene contained on plasmid pSR 2-4.

CLAIMS:

CLMS(10)

10. **Transformed** whole **plants**, said **transformed** whole **plants** being other than solanaceous **plants**, said **transformed** whole **plants** comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimetic gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase and one or more **lysozyme** genes, and said **transformed** **plants**, as a result of being **transformed** with said **lysozyme** gene structures, exhibiting an increased resistance to said fungus as compared to a **plant** of the same **plant** species which is not so **transformed**.

CLAIMS:

CLMS(11)

11. **Transformed** whole **plants** according to claim 10 wherein the **lysozyme** gene is of non-**plant** origin.

CLAIMS:

CLMS(12)

12. **Transformed** whole **plants** according to claim 10 wherein the **lysozyme** gene is selected from a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene and combinations thereof.

CLAIMS:

CLMS(13)

13. **Transformed** whole **plants** according to claim 10 wherein the **lysozyme** gene structure a) is contained on plasmid pSR 2-4 or b) is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene contained on plasmid pSR 2-4.

CLAIMS:

CLMS(14)

14. **Transformed** **plant** parts, said **transformed** **plant** parts being of a **plant** other than a solanaceous **plant**, said **transformed** **plant** parts comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimetic gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase and one or more **lysozyme** genes, and said **transformed** **plant** part, as a result of being **transformed** with said **lysozyme** gene structures, exhibiting an increased resistance to said fungus as compared to a **plant** part of the same **plant** species and part type which is not so **transformed**.

CLAIMS:

CLMS(16)

16. **Transformed** **plant** parts according to claim 14 wherein the **lysozyme** gene is of non-**plant** origin.

CLAIMS:

CLMS(17)

17. **Transformed** **plant** parts according to claim 14 wherein the **lysozyme** gene is selected from a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene and combinations thereof.

CLAIMS:

CLMS(18)

18. **Transformed** **plant** parts according to claim 14 wherein the **lysozyme** gene structure a) is contained on plasmid pSR 2-4 or b) is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene contained on plasmid pSR 2-4.

CLAIMS:

CLMS(19)

19. A method for **transforming** a **plant** cell to confer on said **plant** cell an increased resistance to a fungus, said **transformed** **plant** cell being of a **plant** other than a solanaceous **plant**, said method comprising introducing into the genome of said **transformed** **plant** cells one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimetic gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase and one or more **lysozyme** genes, and said **transformed** **plant** cell, as a result of being **transformed** with said **lysozyme** gene structures, exhibiting an increased resistance to said fungus as compared to a **plant** cell of the same **plant** species and cell type which is not so **transformed**.

L5: 12 of 18

TITLE: Transgenic plants containing multiple disease resistance genes

US PAT NO: 5,530,187 DATE ISSUED: Jun. 25, 1996
:IMAGE AVAILABLE:

APPL-NO: 08/093,372 DATE FILED: Jul. 16, 1993

US PAT NO: 5,530,187 :IMAGE AVAILABLE: L5: 12 of 18
DATE ISSUED: Jun. 25, 1996
TITLE: Transgenic plants containing multiple disease resistance genes

INVENTOR: Christopher J. Lamb, San Diego, CA
Qun Zhu, San Diego, CA
Eileen A. Maher, Madison, WI
Richard A. Dixon, Ardmore, OK

ASSIGNEE: The Salk Institute for Biological Studies, La Jolla, CA (U.S. corp.)

APPL-NO: 08/093,372
DATE FILED: Jul. 16, 1993
ART-UNIT: 183
PRIM-EXMR: David T. Fox
LEGAL-REP: Stephen E. Reiter, Robert T. Ramos

ABSTRACT:
In accordance with the present invention, there are provided transgenic plants comprising a plurality of plant-defense-associated proteins that

are expressed to produce such proteins in an amount sufficient to increase the plants resistance to plant pathogens, relative to non-transgenic plants of the same species. The transgenic plants are useful to study patterns of development, and to provide increased resistance to plant pathogens when grown in crops as a food source, and the like. Nucleic acid constructs are also provided that are useful in methods for producing the invention transgenic plants.

DETDESC:

DETD(16)

Suitable "**plant**-defense-associated-proteins" contemplated for use in the invention **transgenic** **plants** are those classes of proteins that are involved in specific **plant** defense mechanism pathways, such as, for example, lytic enzymes, thaumatine-like proteins, .alpha.-thionin (e.g., Bohlmann et al., EMBO J., 7:1559-1565, 1988), zeamatin (e.g., Vigers et al., Mol. **Plant** Micro. Interactions, 4:315-323, 1991) pathogenesis-related (PR) proteins (e.g., Bol et al., Ann. Rev. Phytopathol., 28:113-138, 1990), ribosome-inactivating-proteins (RIPs) (e.g., Leach et al., J. Biol. Chem., 266:1564-1573, 1990), lectins (e.g., Moreno et al., PNAS, USA, 86:7885-7889, 1989), cecropins, non-**plant** **lysozymes**, the Bacillus thuringensis toxin, enzymes involved in phytoalexin biosynthesis, proteinase inhibitors (e.g., Garcia-Olmedoz et al., Surv. **Plant** Mol. Cell Biol., 4:275-334, 1987), inducers of **plant** disease resistance mechanisms, and the like.

L5: 13 of 18

TITLE: Protection of plants against plant pathogens
US PAT NO: 5,422,108 DATE ISSUED: Jun. 6, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/798,223 DATE FILED: Nov. 25, 1991
REL-US-DATA: Continuation of Ser. No. 762,679, Sep. 19, 1991, abandoned.

US PAT NO: 5,422,108 :IMAGE AVAILABLE: L5: 13 of 18
DATE ISSUED: Jun. 6, 1995
TITLE: Protection of plants against plant pathogens
INVENTOR: T. Erik Mirkov, San Diego, CA
Leona C. Fitzmaurice, San Diego, CA
ASSIGNEE: Smart Plants International Inc., Madison, WI (U.S. corp.)
APPL-NO: 07/798,223
DATE FILED: Nov. 25, 1991
ART-UNIT: 188
PRIM-EXMR: Douglas W. Robinson
ASST-EXMR: Jean C. Witz
LEGAL-REP: Spensley Horn Jubas & Lubitz

ABSTRACT:
Transgenic **plants** that express properly processed ruminant or ruminant-like **lysozymes** and that are resistant to bacterial pathogens, including both gram-negative and gram-positive bacteria, are provided. A preferred embodiment provides **transgenic** tobacco **plants** that express a sufficient concentration of properly processed bovine **lysozyme** c2 to render the **plants** less susceptible to bacterial **plant** pathogens.
Methods and compositions for treatment of plants, seeds and other plant tissues prior to or after exposure or infection with bacterial plant pathogens are also provided. In particular, compositions and methods of contacting plants with such compositions that contain a concentration of bovine lysozyme c2 or other ruminant or ruminant-like lysozyme are provided.
A signal sequence that is effective for properly processing heterologous proteins that are expressed in transgenic plants is also provided.

ABSTRACT:
Transgenic **plants** that express properly processed ruminant or ruminant-like **lysozymes** and that are resistant to bacterial pathogens, including both gram-negative and gram-positive bacteria, are provided. A preferred embodiment provides **transgenic** tobacco **plants** that express a sufficient concentration of properly processed bovine **lysozyme** c2 to render the **plants** less susceptible to bacterial **plant** pathogens.
Methods and compositions for treatment of plants, seeds and other plant tissues prior to or after exposure or infection with. . .

SUMMARY:

BSUM(2)

This invention is directed to **transgenic** **plants** that include heterologous DNA that encodes a ruminant **lysozyme**, that is expressed in the **plant** and that thereby provides protection against diseases caused by **plant** pathogens, particularly **plant** bacterial pathogens. This invention is also directed to seeds that are coated with a composition that contains a ruminant **lysozyme** and to methods of treating **plants**, cut flowers, fruits, seeds and other **plant** tissues, which are infected with one or more **plant** pathogens or which are susceptible to such infection, by contacting the **plants**, flowers, fruits or seeds with a ruminant **lysozyme** in order to treat them for diseases caused by **plant** pathogens or to make them less susceptible or resistant to diseases caused by **plant** pathogens. This invention is also directed to methods for producing a ruminant **lysozyme** from **transgenic** **plants** that express the **lysozyme** and to peptides that direct proper processing of heterologous proteins in **transgenic** **plants**.

SUMMARY:

BSUM(43)

Transgenic **plants** that are resistant to or are less susceptible to diseases caused by **plant** pathogens are provided. In particular, **transgenic** **plants**, including crop **plants**, such as tobacco, tomato, potato, rice, corn, cotton and others, that express heterologous DNA that encodes a ruminant **lysozyme** or other unusually stable **lysozyme** and that are thereby rendered resistant or less susceptible to diseases caused by **plant** pathogens, particularly common bacterial pathogens, such as species of Pseudomonas, Agrobacterium, Xanthomonas, Erwinia and Clavibacter, are provided. In preferred embodiments, **transgenic** **plants** that express DNA that encodes bovine **lysozyme** c are provided.

SUMMARY:

BSUM(46)

Methods for producing ruminant and ruminant-like **lysozyme** by developing **transgenic** **plants** that express and properly process the respective **lysozyme**, **planting**, growing, then harvesting the **transgenic** **plants** and isolating the **lysozyme** from the **plants** are provided.

SUMMARY:

BSUM(47)

Finally, a signal sequence that effects proper processing of heterologous genes in **transgenic** **plants** and method for producing authentically processed heterologous proteins by growing **transgenic** **plants** are also provided. In preferred embodiments, the DNA encoding the bovine **lysozyme** c signal peptide, which is set forth in Sequence ID No. 2 and which is effective for directing proper processing of bovine **lysozyme** c2 in **transgenic** **plants**, is linked to DNA encoding other proteins and introduced into **plants** in order to produce properly processed proteins that are encoded by the heterologous DNA.

SUMMARY:

BSUM(49)

Transgenic **plants** that express DNA that encodes a ruminant or ruminant-like **lysozyme** and that are resistant to infection by certain microbes are produced. Such **plants** include, but are not limited to, tomato, potato, rice, tobacco and other crop **plants**. In preferred embodiments, **transgenic** tobacco **plants** that express sufficient concentrations of bovine **lysozyme** c to inhibit the growth of **plant** bacterial pathogens have been developed.

SUMMARY:

BSUM(50)

The **transgenic** tobacco, tomato and potato **plants**, which include DNA encoding bovine **lysozyme** c in their genomes, have been prepared by introducing DNA encoding the precursor of bovine **lysozyme** c, which includes the native signal sequence, into the genomes of **plants** using Agrobacterium Ti plasmid-based procedures.

SUMMARY:

BSUM(51)

The **transgenic** tobacco **plants** appear to express sufficient concentrations of mature, properly processed, bovine **lysozyme** c to render them less susceptible to **plant** bacterial pathogens, including gram-negative bacterial pathogens.

DETDESC:

DETD(18)

The signal sequences and processing sites contemplated for use herein are those that effect processing of **lysozyme** in **transgenic** **plants** and also in host cells, such as P. patoris. Any peptide or DNA encoding such peptide that effects proper processing in **plant** hosts is contemplated for use herein. Preferred signal peptides and DNA encoding signal peptides are those that effect proper processing in both the selected **plant** host and in host cells in culture. The bovine

lysozyme c signal peptide and variants thereof that effect proper processing in both **transgenic** **plant** hosts and cultured host cells constitutes the preferred signal sequence.

DETDESC:

DETD(35)

When engineering a disease- or pathogen-resistant **plant**, the selected promoter should be sufficiently efficient so that at least an adequate amount of the heterologous gene product, such as **lysozyme**, is expressed to render the **plant** less susceptible to the disease caused by the **plant** pathogen, but not enough to cause deleterious effects in the **plant**. In embodiments in which the **plant** or seed is used as a source of the heterologous gene product, expression should be maximized, but the amount of gene product expressed should not substantially affect the yield or health of the **transgenic** **plant** in which it is expressed.

DETDESC:

DETD(47)

Both purified **lysozyme** and DNA encoding a **lysozyme** or **transgenic** **plants** that express a heterologous **lysozyme** are required for practice of the methods described herein. Purified **lysozyme** is required for methods of treating **plants**, seeds and cut flowers and other **plant** tissues by contacting them with an effective concentration of **lysozyme**. DNA encoding a **lysozyme** is used for constructing **transgenic** **plants** that are of reduced susceptibility or are resistant to particular **plant** pathogens or for preparing host cells that are cultured in vitro in order to produce the **lysozyme** for use in treating **plants**, **plant** tissues and seeds or to replicate DNA for use in preparing **transgenic** **plants**.

DETDESC:

DETD(49)

DNA encoding the particular **lysozyme** may be obtained by any method known to those of skill in the art. For example, DNA probes may be synthesized based on a partial amino acid sequence of a selected **lysozyme** or a **lysozyme** from a related species and used to screen a suitable recombinant DNA library. Alternatively, DNA may be synthesized based on a known amino acid sequence of a **lysozyme**. DNA constructs that include suitable promoters and other regulatory regions may be inserted into suitable vectors, plasmids or expression vectors for introduction into host cells to produce the **lysozyme** by culturing the host cells or for introduction into **plant** cells to produce **transgenic** **plants**.

DETDESC:

DETD(52)

DNA fragments that encode a particular ruminant or ruminant-like **lysozyme** c may be prepared by chemical synthesis or by reverse transcription of messenger RNA (mRNA) corresponding to **lysozyme**-encoding DNA into complementary DNA (cDNA) followed by conversion of the cDNA into double-stranded cDNA. Genomic DNA may also be obtained. . . with probes derived from the cDNA or by other methods well-known to those of skill in the art. If the **lysozyme** is sufficiently stable to be suitable for treating **plants** and **plant** tissues, it may be produced in cell or tissue culture or in other hosts, such as **transgenic** **plants** and animals. Alternatively, the DNA may be introduced into a **plant** to produce a **transgenic** **plant** that is resistant to or less susceptible to bacterial **plant** pathogens.

DETDESC:

DETD(57)

Preferred DNA constructs herein contain DNA that includes a sequence of nucleotide base pairs which encodes bovine pre-**lysozyme** c2 (with either histidine or lysine, but preferably histidine, at position 98 of the mature protein portion) or a **lysozyme** that has substantially the same lytic activity and stability as bovine **lysozyme** c and is capable, upon **transformation** into a **plant**, of expression and proper processing, such that the resulting **transgenic** **plant** is resistant or less susceptible to a broad spectrum of **plant** bacterial pathogens, including both gram-negative and gram-positive pathogens. Other preferred constructs include those that are capable, upon **transformation** of a host, such as P. pastoris, of directing expression and proper processing of stable and biologically active **lysozyme**.

DETDESC:

DETD(72)

Immunoassays and radioimmunoassays, such as those described below in Example 1, may be used to further characterize the **lysozyme**. The **lysozyme** is then tested to determine if it meets criteria for use in treating **plants** or for expression in **transgenic** **plants** to render them resistant to certain pathogens. The key parameters include the ability to lyse gram-negative **plant** pathogens, such as Erwinia carotovora, and stability either under field or greenhouse conditions or other conditions under which **plant** tissues, such as seeds, are coated or contacted with the **lysozyme**. The ability to lyse gram-negative **plant** bacteria may be tested in accordance with any method known to those of skill in the art, including kill curves. . . following one to three hours at 30.degree. C. or 37.degree. C., or other measurements that reflect the ability of the **lysozyme** to withstand the conditions under which it is used to control or eradicate **plant** pathogens. **Lysozyme** suitable for use herein is stable following exposure to such conditions.

DETDESC:

DETD(73)

The selected **lysozyme** may then be used for treating **plants**, seeds, cut flowers and **plant** tissues as described herein, and DNA encoding the **lysozyme** may be introduced into **plants** to produce bacterial pathogen-resistant **transgenic** **plants** as described above.

DETDESC:

DETD(91)
Preparation of **Lysozyme** from **Transgenic** **Plants**

DETDESC:

DETD(93)

Transgenic **plants**, such as tomato, tobacco, rice and potato, are produced and tested to assess expression of and activity of the **lysozyme** produced in the **plant**. Any method known to those of skill in the art for assessing such expression may be used. Sample assays are. . .

DETDESC:

DETD(94)

Once expression of the **lysozyme** is verified, the **plants** may be sexually propagated by crossing with a non-**transgenic** **plant** or a **transgenic** **plant** to produce seeds that germinate into disease-resistant **plants**.

DETDESC:

DETD(95)

Alternatively, the **transgenic** **plants**, or seeds therefrom, may be **planted**, grown and harvested to serve as a source of the **lysozyme** that is expressed in the **plant**. The **lysozyme** is then isolated and purified, using standard protein purification methodology, from the harvested **plants** (see, e.g., Hughes et al. (1991) Biopharm. May 1991:18-28).

DETDESC:

DETD(98)

The procedures used to clone and express DNA encoding bovine **lysozyme** precursor in methylotrophic host cells are described as a model for the cloning and expression of any ruminant or ruminant-like **lysozyme**. Any suitable host cells, particularly eukaryotic host cells, and any methods for cloning or synthesizing DNA and expressing the DNA may be used to obtain DNA for preparing **transgenic** **plants** that express **lysozyme** and to produce **lysozyme**.

DETDESC:

DETD(110)

The DNA encoding bovine **lysozyme** c that was subsequently used for preparing **transgenic** **plants** was the insert, for which the sequence is set forth in Seq. ID No. 1, from BL3, but modified as. . . to include DNA encoding Met and Lys immediately before the Ala, so that the resulting DNA encodes the entire bovine **lysozyme** precursor. The DNA was also further modified by removal of the 3' untranslated sequence.

DETDESC:

DETD(155)
Preparation of **Transgenic** Tobacco, Tomato, Potato and Rice **Plants** **Transformed** with DNA that Encodes Bovine **Lysozyme** Precursor

DETDESC:

DETD(162)

B. Preparation of **Transgenic** Tobacco **Plants** that Express Bovine **Lysozyme**

DETDESC:

DETD(164)

Eleven of the 100 kanamycin-resistant tobacco **plants** in culture were randomly selected and tested for the production of bovine **lysozyme** by immunoblot analysis. Extracts were prepared by grinding the tissue (100 mg) in liquid nitrogen and adding 250 .mu.l 10.25M. . . . was loaded per lane of a 10% polyacrylamide gel containing 0.1% SDS (Laemmli (1970) Nature 227:680-685). An extract from a non-**transformed** **plant** and 50 ng of purified E- pastoris-produced bovine **lysozyme** were included as controls.

DETDESC:

DETD(165)

The . . . the proteins were electrotransferred to a nitrocellulose membrane, and the membrane was exposed to polyclonal rabbit antisera raised against bovine **lysozyme** and reacted with goat anti-rabbit IgG antisera conjugated to alkaline phosphatase. The proteins that reacted with the antibodies were detected using the Western Blot Alkaline Phosphatase system of Promega (Madison, Wis.). Each of the **transgenic** **plants** expressed varying amounts of the P. pastoris-produced bovine **lysozyme**.

DETDESC:

DETD(166)

Comparison of the size of the bovine **lysozyme** protein expressed in the **plants** with that expressed in P. pastoris indicated that the signal sequence was correctly cleaved in the **transgenic** tobacco **plants**.

DETDESC:

DETD(203)
Transgenic Tobacco **Plants** that Express Bovine **Lysozyme** c were Less Susceptible to Bacterial Infection than **Plants** that do not Express Bovine **Lysozyme** c2

DETDESC:

DETD(204)

Four **transgenic** tobacco **plants** that express bovine **lysozyme** c.sup.2 were transferred from tissue culture to soil and maintained in a growth chamber. Two untransformed tobacco **plants**, and one **plant** that expressed the GUS gene under the control of the CaMV 35S promoter, were also transferred into soil in the. . .

DETDESC:

DETD(206)

The results, showing the numbers of lesions on the four **transgenic** **plants** that express bovine **lysozyme** c2 and the three control **plants**, are set forth in Table 5.

DETDESC:

DETD(207)

TABLE 5

Plant	Total No. lesions	No. leaves contacted per leaf
Untransformed		
	196	8 24.5
Untransformed		
	246	8 30.8
Transformed	72	8 7.2
CaMV 35S-GUS		
Transformed #1		
	13	10 1.5
CaMV 35S-**lysozyme**		
Transformed #2		
	3	9 3
CaMV 35S-**lysozyme**		
Transformed #3		
	63	8 7.8
CaMV 35S-**lysozyme**		
Transformed #4		
	168	3 56
CaMV 35S-**lysozyme**		

DETDESC:

DETD(208)

Three of the four **plants** that expressed bovine **lysozyme** c2 (**transformant** Nos. 1-3) developed substantially fewer lesions than the two untransformed **plants**.

L5: 14 of 18

TITLE: Rice chitinase promoter
US PAT NO: 5,399,680 DATE ISSUED: Mar. 21, 1995
:IMAGE AVAILABLE:
APPL-NO: 07/704,288 DATE FILED: May 22, 1991

US PAT NO: 5,399,680 :IMAGE AVAILABLE: L5: 14 of 18
DATE ISSUED: Mar. 21, 1995
TITLE: Rice chitinase promoter
INVENTOR: Qun Zhu, San Diego, CA
Christopher J. Lamb, San Diego, CA
ASSIGNEE: The Salk Institute for Biological Studies, La Jolla, CA (U.S. corp.)
APPL-NO: 07/704,288
DATE FILED: May 22, 1991
ART-UNIT: 183
PRIM-EXMR: David T. Fox
ASST-EXMR: Mary E. Mosher
LEGAL-REP: Pretty, Schroeder, Brueggemann & Clark

ABSTRACT:
Novel chitinase gene, and its associated regulatory region, from a monocotyledon plant is described.

DETDESC:

DETD(69)

A . . . respectively. These plasmids were transferred into Escherichia coli strain HB101 by the CaCl.sub.2 method :Maniatis et al. supra:, and the **transformed** cells grown to stationary phase at 37.degree. C. in LB broth. The cells were then inoculated into 5 ml of. . . harvested and lysed by sonication in 10 mM TRIS-HCl, pH 8.0, 50 mM EDTA, 8% sucrose, 0.5% Triton X-100, and **lysozyme** (2 mg/ml). Soluble bacterial extracts were analyzed in a 10% SDS-polyacrylamide gel :Maniatis et al. supra:. Immunoblotting was performed as described by Bradley et al., **Planta** 173:149-160 (1988). Antiserum to bean chitinase, prepared employing standard techniques, was obtained as a gift from T. Boller.

L5: 15 of 18

TITLE: Use of lysozyme gene structures in plants to increase resistance
US PAT NO: 5,349,122 DATE ISSUED: Sep. 20, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/555,557 DATE FILED: Jul. 19, 1990
FRN-PR. NO: 3926390 FRN FILED: Aug. 10, 1989
FRN-PR. CO: Federal Republic of Germany

US PAT NO: 5,349,122 :IMAGE AVAILABLE: L5: 15 of 18
DATE ISSUED: Sep. 20, 1994
TITLE: Use of lysozyme gene structures in plants to increase resistance
INVENTOR: Rudiger Hain, Langenfeld, Federal Republic of Germany
Klaus Stenzel, Duesseldorf, Federal Republic of Germany
ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Federal Republic of Germany (foreign corp.)
APPL-NO: 07/555,557
DATE FILED: Jul. 19, 1990
ART-UNIT: 184
PRIM-EXMR: David T. Fox
LEGAL-REP: Sprung Horn Kramer & Woods

ABSTRACT:
A method for increasing the resistance of a plant to fungi and animal pests comprising introducing into the genome of the plant one or more lysozyme gene structures which express lysozyme, the lysozyme gene structure comprises a chimeric gene fusion of the TR promoter, the signal peptide sequence of barley alpha-amylase and one or more lysozyme genes.

SUMMARY:

BSUM(4)

Patent application WO 89/04371 describes the **transformation** of **plants** having specific **lysozyme** genes for increasing the resistance to specific bacteria.

SUMMARY:

BSUM(60)

Transformed **plant** cells (including protoplasts) and **plants** (including seeds and parts of **plants**) which have an increased resistance to fungi and animal pests and which contain one or more of the **lysozyme** gene structures, as well as those **transformed** **plant** cells and **plants** which can be obtained by the above method, are also a subject of the present invention.

SUMMARY:

BSUM(62)

(a) use of **lysozyme** gene structures which consist of chimeric gene fusions of the TR promoter, the signal peptide sequence of barley alpha-amylase and one or more **lysozyme** genes or contain these chimeric gene fusions and the use of vectors and of **transformed** microorganisms according to the invention which contain the **lysozyme** gene structure, for **transforming** **plant** cells (including protoplasts) and **plants** (including seeds and parts of **plants**) with the result of an increased resistance to fungi and animal pests, as well as the

SUMMARY:

BSUM(71)

For . . . derivatives thereof (Zambryski et al. 1983), with customary methods (for example, Van Haute et al. 1983). The success of the **transformation** can be checked by detecting nopaline or NPT(II). Alternatively, the **lysozyme** gene structure can be cloned in a binary vector (for example, Koncz and Schell 1986) and transferred as described above to a suitable Agrobacterium strain (Koncz and Schell 1986). The resulting Agrobacterium strain, which contains the **lysozyme** gene structure into a form which can be transferred into **plants**, is used further for **transforming** **plants**.

SUMMARY:

BSUM(74)

Transformed (**transgenic**) **plants**, or **plant** cells, are prepared by known methods, for example by leaf-disc **transformation** (for example Horsch et al. 1985), by coculturing regenerating **plant** protoplasts or cell cultures with Agrobacterium tumefaciens (for example Matron et al. 1979, Hain et al. 1985), or by direct DNA-transfection. Resulting **transformed** **plants** are detected either by selection for reporter gene expression, for example, by phosphorylation of kanamycin sulphate in vitro (Reis et. . . 1984; Schreier et al. 1985), or by the expression of nopalin synthase (according to Aerts et al. 1983) or of **lysozyme** by Northern-blot analysis and Western blot analysis. It is also possible to detect the **lysozyme** in **transformed** **plants** in a known manner using specific antibodies.

SUMMARY:

BSUM(76)

The **transformed** **plant** cells as well as the **transformed** **plants** which contain **lysozymes**, show a considerably better resistance to phytopathogenic fungi and animal pests, in particular to insects, mites and nematodes.

DETDESC:

DETD(61)

In the **plant** cells and **plants** obtained according to the above examples, the presence of the **lysozyme** gene was confirmed by Southern blot analysis. The expression of the **lysozyme** gene was detected by Northern blot analysis and **lysozyme** with the aid of specific antibodies. **Transformed** and non-**transformed** **plants** (for comparison) were sprayed with a spore suspension of Botrytis cinera and Alternaria longipes, and infestation with the fungus was scored 1 week later. Compared with the non-**transformed** comparison **plants**, the **transformed** **plants** showed an increased resistance to infestation with fungus.

DETDESC:

DETD(67)

TABLE I

Effect of the **lysozyme** gene on the infestation of the tobacco **plants** with Alternaria longipes

Plant	% infested leaf area on leaf 1	2	3	4	x	Reduction*
SR.sub.1 wild type	40	43	35	33	38	--
Transformed **plant**	14	11	2	2	7	82%

*Reduction calculated with Abbott's formula

DETDESC:

DETD(68)

TABLE II

Effect of the **lysozyme** gene on the infestation of the tobacco **plants** with Botrytis cinerea

Plant	% infested leaf area on leaf 1	2	3	4	x	Reduction
SR.sub.1 wild type	100	100	100	100	100	--
Transformed **plant**	23	35	23	30	28	72%

*Reduction calculated by Abbott's formula

DETDESC:

DETD(89)

The following literature references can be cited in connection with the **transformation** of **plants** or **plant** cells and with **lysozyme** genes which can be used according to the invention:

CLAIMS:

CLMS(5)

5. **Transformed** cells of **plants**, said **transformed** cells of **plants** having an increased resistance to fungi, said **transformed** cells of **plants** comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimeric gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase, and one or more **lysozyme** genes, and said **plants** being selected from the group consisting of potato, and tomato.

CLAIMS:

CLMS(7)

7. **Transformed** cells of **plants** according to claim 5, wherein the **lysozyme** gene structure comprises a **lysozyme** gene of non-**plant** origin.

CLAIMS:

CLMS(8)

8. **Transformed** cells of **plants** according to claim 5, wherein the **lysozyme** gene structure comprises a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene, or a combination thereof.

CLAIMS:

CLMS(9)

9. **Transformed** cells of **plants** according to claim 5, wherein the **lysozyme** gene structure is contained on plasmid pSR 2-4, or the **lysozyme** gene structure is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene structure contained on plasmid pSR 2-4.

CLAIMS:

CLMS(10)

10. **Transformed** whole **plants**, said **transformed** whole **plants** having an increased resistance to fungi, said **transformed** whole **plants** comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimeric gene fusion of

the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase, and one or more **lysozyme** genes, and said **plants** being selected from the group consisting of potato, and tomato.

CLAIMS:

CLMS(11)

11. **Transformed** whole **plants** according to claim 10, wherein the **lysozyme** gene structure comprises a **lysozyme** gene of non-**plant** origin.

CLAIMS:

CLMS(12)

12. **Transformed** whole **plants** according to claim 10, wherein the **lysozyme** gene structure comprises a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene, or a combination thereof.

CLAIMS:

CLMS(13)

13. **Transformed** whole **plants** according to claim 10, wherein the **lysozyme** gene structure is contained on plasmid pSR 2-4, or the **lysozyme** gene structure is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene structure contained on plasmid pSR 2-4.

CLAIMS:

CLMS(14)

14. **Transformed** **plant** parts, said **transformed** **plant** parts having an increased resistance to fungi, said **transformed** **plant** parts comprising in their genome one or more **lysozyme** gene structures, said **lysozyme** gene structures expressing **lysozyme**, said **lysozyme** gene structures comprising a chimeric gene fusion of the TR promoter, the signal peptide-encoding sequence of barley alpha-amylase, and one or more **lysozyme** genes, and said **plants** being selected from the group consisting of potato, and tomato.

CLAIMS:

CLMS(16)

16. **Transformed** **plant** parts according to claim 14, wherein the **lysozyme** gene structure comprises a **lysozyme** gene of non-**plant** origin.

CLAIMS:

CLMS(17)

17. **Transformed** **plant** parts according to claim 14, wherein the **lysozyme** gene structure comprises a chicken albumen **lysozyme** gene, a T4-phage **lysozyme** gene, or a combination thereof.

CLAIMS:

CLMS(18)

18. **Transformed** **plant** parts according to claim 14, wherein the **lysozyme** gene structure is contained on plasmid pSR 2-4, or the **lysozyme** gene structure is a DNA sequence which acts essentially in the same manner as the **lysozyme** gene structure contained on plasmid pSR 2-4.

L5: 16 of 18

TITLE: Process for secretory production of a calcium-binding protein
US PAT NO: 5,288,623 DATE ISSUED: Feb. 22, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/912,582 DATE FILED: Jul. 13, 1992
FRN-PR. NO: 1-279528 FRN FILED: Oct. 26, 1989
FRN-PR. CO: Japan
REL-US-DATA: Continuation of Ser. No. 587,843, Sep. 25, 1990, abandoned.

US PAT NO: 5,288,623 :IMAGE AVAILABLE: L5: 16 of 18
DATE ISSUED: Feb. 22, 1994
TITLE: Process for secretory production of a calcium-binding protein
INVENTOR: Shuhei Zenno, Yokohama, Japan
Satoshi Inouye, San Diego, CA
ASSIGNEE: Chisso Corporation, Osaka, Japan (foreign corp.)
APPL-NO: 07/912,582
DATE FILED: Jul. 13, 1992
ART-UNIT: 182
PRIM-EXMR: Robert J. Hill, Jr.
ASST-EXMR: John D. Ulm
LEGAL-REP: Wenderoth, Lind & Ponack

ABSTRACT:
A process for secretory production of a calcium-binding protein very useful for producing heterogenic proteins in Escherichia coli according to gene recombinant technique is provided, which process comprises using Escherichia coli and using a secretory expression system with the promoter of lipoprotein and the gene of signal peptide of outer membrane protein A, according to recombinant DNA technique.

DETDESC:

DETD(34)

Colony of **transformant** containing variant aequorin secretory expression vector was **planted** on 5 ml LB medium and cultured at 30.degree. C. overnight. The resulting culture solution (1.5 ml) was transferred into. . . glucose solution (60 .mu.l) (50 mM glucose, 25 mM Tris.HCl (pH 8.0) and 10 mM EDTA), adding a 10 mg/ml **lysozyme** solution (40 .mu.l) (prepared with a glucose solution just before its use), mildly mixing, allowing the mixture to stand at. . .

L5: 17 of 18

TITLE: Porous glass fibers with immobilized biochemically active material
US PAT NO: 4,748,121 DATE ISSUED: May 31, 1988
:IMAGE AVAILABLE:
APPL-NO: 06/677,108 DATE FILED: Nov. 30, 1984

US PAT NO: 4,748,121 :IMAGE AVAILABLE: L5: 17 of 18
DATE ISSUED: May 31, 1988
TITLE: Porous glass fibers with immobilized biochemically active material
INVENTOR: Richard P. Beaver, Library, PA
Ronald E. Betts, Turtle Creek, PA
Lin-Chang Chiang, Export, PA
George V. Sanzero, New Kensington, PA
ASSIGNEE: PPG Industries, Inc., Pittsburgh, PA (U.S. corp.)
APPL-NO: 06/677,108
DATE FILED: Nov. 30, 1984
ART-UNIT: 128
PRIM-EXMR: David M. Naff
LEGAL-REP: Kenneth J. Stachel

ABSTRACT:
Biochemically active material is immobilized on porous silica-rich glass fibers having a diameter of about 3 to 150 microns, a length of about 0.03 inch to continuous fiber length, a mean pore diameter in the range of about 10 to 3000 angstroms, a pore volume of about 0.5 to 1.5 cc/gm and a surface area of about 10 to 600 m.sup.2 /gm. The porous glass fibers are preferably formed from a composition containing greater than 35 up to 60 weight percent B.sub.2 O.sub.3, about 1 to 10 weight percent alkali metal oxides, about 30 to 65 weight percent SiO.sub.2, up to about 5 weight percent ZrO.sub.2, and up to about 4 weight percent Al.sub.2 O.sub.3. Fibers having the composition are heated to cause phase separation into a boron-rich phase and a silica-rich phase, and are then treated by water and acid leaching to produce the porous glass fibers. A biochemically active material is attached to the fibers by absorption or by covalent bonding with a linking agent.

DETDESC:

DETD(3)

The . . . activity or production capability. Nonexclusive examples of the biochemically active material include proteins; nucleic acids; nucleoproteins; polynucleotides; polynucleosides; lipoproteins; isozymes; **lysozymes**; co-enzymes including co-factors and prosthetic groups; hormones; endorphins; enkaphlins; peptides; apoenzymes; organic or inorganic matter constituting substrates for enzymes; hybridomas,. . . antibodies; antigens; immunoglobulins; antigen-antibody complexes; lymphokines; and other immunological material; viruses; plasmids; growth factors; antibiotics; and living, dead and genetically **transformed** prokaryotic and eukaryotic cells such as bacterial, yeast, mold, fungi, **plant**, and animal cells including mammalian cells; bound dependent cells such as cells from insects, fish, reptiles, aves, mammals and other. . .

L5: 18 of 18

TITLE: Novel lysozyme-sensitive microorganism
US PAT NO: 4,681,847 DATE ISSUED: Jul. 21, 1987
:IMAGE AVAILABLE:
APPL-NO: 06/695,574 DATE FILED: Jan. 28, 1985
FRN-PR. NO: 56-65777 FRN FILED: Apr. 30, 1981
FRN-PR. CO: Japan
FRN-PR. NO: 56-151464 FRN FILED: Sep. 25, 1981

FRN-PR. CO: Japan
REL-US-DATA: Continuation of Ser. No. 372,129, Apr. 27, 1982, abandoned.

US PAT NO: 4,681,847 :IMAGE AVAILABLE: L5: 18 of 18
DATE ISSUED: Jul. 21, 1987
TITLE: Novel lysozyme-sensitive microorganism
INVENTOR: Ryoichi Katsumata, Machida, Japan
Tetsuo Oka, Yokohama, Japan
Akira Furuya, Kawasaki, Japan
ASSIGNEE: Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan (foreign corp.)
APPL-NO: 06/695,574
DATE FILED: Jan. 28, 1985
ART-UNIT: 127
PRIM-EXMR: James Martinell
LEGAL-REP: Antonelli, Terry & Wands

ABSTRACT:
A novel lysozyme-sensitive microorganism belonging to the genus Corynebacterium or Brevibacterium and having a sensitivity to lysozyme at a concentration of less than 25 .mu.g/ml is provided from selected mutants. This novel microorganism is especially suitable for use in recombinant DNA technology.

SUMMARY:

BSUM(55)

Application . . . by the amplification of the genetic information, thereby increasing the production of useful substances. Also the genes of animal and **plant** can be cloned, so that useful polypeptides can be produced in these bacteria species by the expression of the genetic information. Thus the application has tremendus industrial importances. The **lysozyme**-ultrasensitive microorganisms of the present invention enable extractive separation of DNA such as plasmid, etc. from the cells and **transformation** of the cells by DNA, and therefore can facilitate application of recombinant DNA technique to the genera Corynebacterium and Brevibacterium.

=> bye
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
U.S. Patent & Trademark Office LOGOFF AT 14:23:23 ON 06 FEB 1998

Welcome to DIALOG

Dialog level 98.01.01D
? b 411;set files biotech

06feb98 15:34:20 User219511 Session D411.2
$0.00 0.008 Hrs File410
$0.00 Estimated cost File410
$0.02 FTSNET
$0.02 Estimated cost this search
$0.05 Estimated total session cost 0.010 Hrs.
File 411:DIALINDEX(R)

DIALINDEX(R)
(c) 1998 Knight-Ridder Info

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
You have 47 files in your file list.
(To see banners, use SHOW FILES command)
? s (transform? or transgen?) and plant? and (lysosom? or or glucocerebro? or iduron?)

Your SELECT statement is:
s (transform? or transgen?) and plant? and (lysosom? or or glucocerebro?
or iduron?)

Items File
----- ----
>>>Operator "OR" in invalid position
? s (transform? or transgen?) and plant? and (lysosom? or glucocerebro? or iduron?)

Your SELECT statement is:
s (transform? or transgen?) and plant? and (lysosom? or glucocerebro? or
iduron?)

Items File
----- ----
6 5: BIOSIS PREVIEWS(R)_1969-1998/Feb W2
3 10: AGRICOLA_70-1998/Jan
1 12: IAC Industry Express (TM)_1995-1998/Feb 06
1 41: Pollution Abs_1970-1998/Jan
5 50: CAB Abstracts_1972-1997/Dec
17 73: EMBASE_1974-1998/Jan W1
3 71: ELSEVIER BIOBASE_1994-1998/Jan W4
3 76: Life Sciences Collection_1982-1997/Dec
1 94: JICST-EPlus_1985-1998/Dec W2
3 144: Pascal_1973-1998/Jan
19 149: IAC(SM)Health&Wellness DB(SM)_1976-1998/Feb W1
9 155: MEDLINE(R)_1966-1998/Mar W4
2 285: BioBusiness(R)_1985-1998/Jan W4
1 315: ChemEng & Biotec Abs_1970-1998/Feb
3 357: Derwent Biotechnology Abs_1982-1998/Feb B2
1 358: Current BioTech Abs_1983-1998/Feb
1 370: Science_1996-1998/Dec W1
1 429: Adis Newsletters(Archive)_1982-1998/Jan 07
41 434: Scisearch(R) Cited Ref Sci_1974-1998/Jan W4
8 636: IAC Newsletter DB(TM)_1987-1998/Feb 06

20 files have one or more items; file list includes 47 files.

? save temp;b 155,5,10,50,73,357;exs;rd

Temp SearchSave "TD465" stored
06feb98 15:37:57 User219511 Session D411.3
$1.98 0.066 Hrs File411
$1.98 Estimated cost File411
$0.20 FTSNET
$2.18 Estimated cost this search
$2.23 Estimated total session cost 0.077 Hrs.

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-1998/Mar W4
(c) format only 1998 The Dialog Corp
*File 155: reloaded for 1998
File 5:BIOSIS PREVIEWS(R) 1969-1998/Feb W2
(c) 1998 BIOSIS
File 10:AGRICOLA 70-1998/Jan
(c) format only 1998 The Dialog Corporation p
File 50:CAB Abstracts 1972-1997/Dec
(c) 1998 CAB International
File 73:EMBASE 1974-1998/Jan W1
(c) 1998 Elsevier Science B.V.
*File 73: EMTAGS no longer in Embase as of 1/98. Type: HELP NEWS 73
for details.
File 357:Derwent Biotechnology Abs 1982-1998/Feb B2
(c) 1998 Derwent Publ Ltd

Set Items Description
--- ----- ----------
Executing TD465
HILIGHT set on as '%'
Processing
546590 TRANSFORM?
77250 TRANSGEN?
3326161 PLANT?
89258 LYSOSOM?
2207 GLUCOCEREBRO?
2767 IDURON?
S1 43 (TRANSFORM? OR TRANSGEN?) AND PLANT? AND (LYSOSOM?
OR
GLUCOCEREBRO? OR IDURON?)
...completed examining records
S2 35 RD (unique items)
? t s2/7/1-35;bye

2/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

08771510 96385336
Role of alveolar macrophages in the dissolution of two different industrial uranium oxides.
Henge-Napoli MH; Ansoborlo E; Claraz M; Berry JP; Cheynet MC
Institut de Protection et de Surete Nucleaire/DPHD/SDOS, Pierrelatte, France.
Cell Mol Biol (Noisy-le-grand) (FRANCE) May 1996, 42 (3) p413-20, Journal Code: BNA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
This study was aimed at assessing and understanding some mechanisms involved in the intracellular particle %transformation% of two uranium oxides (U3O8 and UO2 + Umetal) produced by a new isotopic enrichment %plant% using laser technology. Instillations were conducted on rats with both uranium compounds and alveolar macrophages were harvested at different dates and prepared in order to be studied using transmission electron microscopy and electron energy loss spectrometry (EELS). The presence of particles in the cells was observed from the first day after instillation, and crystalline needles of uranyl phosphate appeared in the cytoplasm of the cells. These needles were more numerous after instillation with the mixture UO2 + Umetal than after administration of U3O8 and may be correlated with the higher solubility of UO2 + Umetal observed in vitro. The formation of insoluble needles in %lysosomes% is consistent with the insolubilisation of uranium observed after phagocytosis by alveolar macrophages.

2/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

08618575 96283392
Bioproduction of human enzymes in %transgenic% tobacco.
Cramer CL; Weissenborn DL; Oishi KK; Grabau EA; Bennett S; Ponce E; Grabowski GA; Radin DN
CropTech Development Corp. Virginia Tech Corporate Research Center, Blacksburg 24060, USA. ccramer@vt.edu
Ann N Y Acad Sci (UNITED STATES) May 25 1996, 792 p62-71, ISSN 0077-8923 Journal Code: 5NM
Contract/Grant No.: R44-NS32369, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
%Transgenic% %plants% have significant potential in the bioproduction of complex human therapeutic proteins due to ease of genetic manipulation, lack of potential contamination with human pathogens, conservation of eukaryotic cell machinery mediating protein modification, and low cost of biomass production. Tobacco has been used as our initial %transgenic% system because Agrobacterium-mediated %transformation% is highly efficient, prolific seed production greatly facilitates biomass scale-up, and development of new "health-positive" uses for tobacco has significant regional support. We have targeted bioproduction of complex recombinant human proteins with commercial potential as human pharmaceuticals. Human protein C (hPC), a highly processed serum protease of the coagulation/anticoagulation cascade, was produced at low levels in %transgenic% tobacco leaves. Analogous to its processing in mammalian systems, tobacco-synthesized hPC appears to undergo multiple proteolytic cleavages, disulfide bond formation, and N-linked glycosylation. Although tobacco-derived hPC has not yet been tested for all posttranslational modifications or for enzymatic (anticlotting) activity, these results are promising and suggest considerable conservation of protein processing machinery between %plants% and animals. CropTech researchers have also produced the human %lysosomal% enzyme %glucocerebrosidase% (hGC) in %transgenic% tobacco. This glycoprotein has significant commercial potential as replacement therapy in patients with Gaucher's disease. Regular intravenous administration of modified %glucocerebrosidase%, derived from human placentae or CHO cells, has proven highly effective in reducing disease manifestations in patients with Gaucher's disease. However, the enzyme is expensive (dubbed the "world's most expensive drug"

by the media), making it a dramatic model for evaluating the potential of %plants% to provide a safe, low-cost source of bioactive human enzymes. %Transgenic% tobacco %plants% were generated that contained the human %glucocerebrosidase% cDNA under the control of an inducible %plant% promoter. hGC expression was demonstrated in %plant% extracts by enzyme activity assay and immunologic cross-reactivity with anti-hGC antibodies. Tobacco-synthesized hGC comigrates with human placental-derived hGC during electrophoretic separations, is glycosylated, and, most significantly, is enzymatically active. Although expression levels vary depending on %transformant% and induction protocol, hGC production of > 1 mg/g fresh weight of leaf tissue has been attained in crude extracts. Our studies provide strong support for the utilization of tobacco for high-level production of active hGC for purification and eventual therapeutic use at potentially much reduced costs. Furthermore, this technology should be directly adaptable to the production of a variety of other complex human proteins of biologic and pharmaceutical interest. (50 Refs.)

2/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

07085518 92288183
Calorimetric and x-ray diffraction studies of rye %glucocerebroside% mesomorphism.
Lynch DV; Caffrey M; Hogan JL; Steponkus PL
Department of Soil, Crop and Atmospheric Science, Cornell University, Ithaca, New York 14853.
Biophys J (UNITED STATES) May 1992, 61 (5) p1289-300, ISSN 0006-3495 Journal Code: A5S
Contract/Grant No.: DK 36849, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
%Glucocerebrosides% (GlcCer) isolated from the leaves of winter rye (Secale cereale L. cv Puma) differ from the more commonly investigated natural and synthetic cerebrosides, in that greater than 95% of the fatty acids are saturated and monounsaturated hydroxy fatty acids. Isomers of the trihydroxy long chain base hydroxysphingenine (t1(8:18 cis or trans)) and isomers of sphingadienine (d18:2(4trans, 8 cis or trans)) comprise 77% and 17%, respectively, of the total long chain bases. The phase behavior of fully hydrated and dry rye leaf GlcCer was investigated using differential scanning calorimetry (DSC) and x-ray diffraction. On initial heating, aqueous dispersions of GlcCer exhibit a single endothermic transition at 56 degrees C and have an enthalpy (delta H) of 46 J/g. Cooling to 0 degrees C is accompanied by a small exothermic transition (delta H = -8 J/g) at 8 degrees C. On immediate reheating, a broad exothermic transition (delta H = -39 J/g) is observed between 10 and 20 degrees C in addition to a transition at 56 degrees C. These transitions are not reversible, and the exothermic transition rapidly diminishes when the sample is held at low temperature. Using x-ray diffraction, it was determined that the endotherm at 56 degrees C represents a transition from a highly ordered lamellar crystalline phase (Lc) with a d-spacing of 57 A and a series of wide-angle reflections in the 3-10 A range, to a lamellar liquid crystalline (L alpha) phase having a d-spacing of 55 A and a diffuse wide-angle scattering peak centered at 4.7 A. Cooling leads to the formation of a metastable gel phase (L beta) with a d-spacing of 64.0 A and a single broad reflection at 4.28 A. Subsequent warming to above 15 degrees C restores the original Lc phase. Thus, rye GlcCer in excess water exhibit a series of irreversible transitions and gel phase metastability. Dry GlcCer undergo an initial heating endothermic transition at 130 degrees C, which is ascribed to a %transformation% into the HII phase from a two phase state characterized by the coexistence of phases with disordered (alpha) and helical (delta) type chain conformations but of unknown lattice identity: An exotherm at 67.5 degrees C observed upon subsequent cooling is of unknown origin. Since an undercooled HII phase persists down to 19 degrees C, the exotherm may derive in part from an alpha-to-delta type chain packing conformational change especially under slow cooling conditions.(ABSTRACT TRUNCATED AT 400 WORDS)

2/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

05709290 89139554
Transport of proteins to the %plant% vacuole is not by bulk flow through the secretory system, and requires positive sorting information.
Dorel C; Voelker TA; Herman EM; Chrispeels MJ
Department of Biology, University of California at San Diego, La Jolla 92093-0116.
J Cell Biol (UNITED STATES) Feb 1989, 108 (2) p327-37, ISSN 0021-9525 Journal Code: HMV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
%Plant% cells, like other eukaryotic cells, use the secretory pathway to target proteins to the vacuolar/%lysosomal% compartment and to the extracellular space. We wished to determine whether the presence of a hydrophobic signal peptide would result in the transport of a reporter protein to vacuoles by bulk flow; to investigate this question, we expressed a chimeric gene in %transgenic% tobacco. The chimeric gene, Phalb, used for this study consists of the 1,188-bp 5' upstream sequence and the hydrophobic signal sequence of a vacuolar seed protein phytohemagglutinin, and the coding sequence of a cytosolic seed albumin (PA2). The chimeric protein PHALB cross-reacted with antibodies to PA2 and was found in the seeds of the %transgenic% %plants% (approximately 0.7% of total protein), but not in the leaves, roots, or flowers. Immunoblot analyses of seed extracts revealed four glycosylated polypeptides ranging in molecular weight from 29,000 to 32,000. The four polypeptides are glycoforms of a single polypeptide of Mr 27,000, and the heterogeneity is due to the presence of high mannose and endoglycosidase H-resistant glycans. The PHALB products reacted with an antiserum specific for complex %plant% glycans indicating that the glycans had been modified in the Golgi apparatus. Subcellular fractionation of glycerol extracts of mature seeds showed that only small amounts of PHALB accumulated in the protein storage vacuoles of the tobacco seeds. In homogenates made in an isotonic medium, very little PHALB was associated with the organelle fraction containing the endoplasmic reticulum and Golgi apparatus; most of it was in the soluble fraction. We conclude that PHALB passed through the Golgi apparatus, but did not arrive in the vacuoles. Transport to vacuoles is not by a bulk-flow mechanism, once proteins have entered the secretory system, and requires information beyond that provided by a hydrophobic signal peptide.

2/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

05677482 90121239
%Plantagoside%, a novel alpha-mannosidase inhibitor isolated from the seeds of %Plantago% asiatica, suppresses immune response.
Yamada H; Nagai T; Takemoto N; Endoh H; Kiyohara H; Kawamura H; Otsuka Y
Oriental Medicine Research Center, Kitasato Institute, Tokyo, Japan.
Biochem Biophys Res Commun (UNITED STATES) Dec 29 1989, 165 (3) p1292-8, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A hot-water extract from the seed of %Plantago% asiatica showed a potent inhibitory activity against jack bean alpha-mannosidase, and a flavanone glucoside, %plantagoside%, was isolated as the inhibitor. %Plantagoside% was a specific inhibitor for jack bean alpha-mannosidase (IC50 at 5 microM) and appeared to be a non-competitive inhibitor of the enzyme. Whereas, negligible or weak inhibitory activities were observed for beta-mannosidase, beta-glucosidase, and sialidase tested. %Plantagoside% also inhibited alpha-mannosidase activities in mouse liver %lysosomal% and microsomal fractions, and the enzyme inhibitory activity in microsomal fraction was enhanced in the presence of glucosidase inhibitor, castanospermine. %Plantagoside% suppressed antibody response to sheep red blood cells and concanavalin A induced lymphocyte proliferation which was measured by [3H]thymidine incorporation.

2/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

05293113 88059230
The %plant% vacuolar protein, phytohemagglutinin, is transported to the vacuole of %transgenic% yeast.
Tague BW; Chrispeels MJ
Department of Biology, University of California, San Diego, La Jolla 92093.
J Cell Biol (UNITED STATES) Nov 1987, 105 (5) p1971-9, ISSN 0021-9525 Journal Code: HMV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Phytohemagglutinin (PHA), the major seed lectin of the common bean, Phaseolus vulgaris, accumulates in the parenchyma cells of the cotyledons. It has been previously shown that PHA is cotranslationally inserted into the endoplasmic reticulum with cleavage of the NH2-terminal signal peptide. Two N-linked oligosaccharide side chains are added, one of which is modified to a complex type in the Golgi apparatus. PHA is then deposited in membrane-bound protein storage vacuoles which are biochemically and functionally equivalent to the vacuoles of yeast cells and the %lysosomes% of animal cells. We wished to determine whether yeast cells would recognize the vacuolar sorting determinant of PHA and target the protein to the yeast vacuole. We have expressed the gene for leukoagglutinating PHA (PHA-L) in yeast under control of the yeast acid phosphatase (PHO5) promoter. Under control of this promoter, PHA-L accumulates to 0.1% of the total yeast protein. PHA-L produced in yeast is glycosylated as expected for a yeast vacuolar glycoprotein. Cell fractionation studies show that PHA-L is efficiently transported to the yeast vacuole. This is the first demonstration that vacuolar targeting information is recognized between two highly divergent species. A small proportion of yeast PHA-L is secreted which may be due to inefficient recognition of the vacuolar sorting signal because of the presence of an uncleaved signal peptide on a subset of the PHA-L polypeptides. This system can now be used to identify the vacuolar sorting determinant of a %plant% vacuolar protein.

2/7/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

05007278 87129338
[Effect of Eleutherococcus on the subcellular structures of the heart in experimental myocardial infarct]
Vliianie eleuterokokka na subkletochnye struktury serdtsa pri eksperimental'nom infarkte miokarda.
Afanas'eva TN; Lebkova NP
Biull Eksp Biol Med (USSR) Feb 1987, 103 (2) p212-5, ISSN 0365-9615 Journal Code: A74
Languages: RUSSIAN Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract
The effect of Eleutherococcus on subcellular heart organization in rats with or without myocardial infarction was investigated. It was found that Eleutherococcus decreases ultrastructural lesions in the ischemic area, intensifies regeneration of subcellular structures and accelerates the recovery after myocardial infarction. The accumulation of glycogen, lipids and %lysosomes% is observed in lipocytes. It is suggested that positive effect of Eleutherococcus during myocardial infarction is related to lipid %transformation% into glycogen.

2/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

04195185 84034197
Phenotype of the accessory cell necessary for mitogen-stimulated T and B cell responses in human peripheral blood: delineation by its sensitivity to the %lysosomotropic% agent, L-leucine methyl ester.
Thiele DL; Kurosaka M; Lipsky PE
J Immunol (UNITED STATES) Nov 1983, 131 (5) p2282-90, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: AM19329, AM, NIADDK; AM09989, AM, NIADDK; AM00599, AM
, NIADDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The %lysosomotropic% compound L-leucine methyl ester (Leu-OMe) was utilized to delineate the phenotype of the accessory cells involved in human B and T cell activation in vitro. Leu-OMe was shown to cause %lysosomal% disruption and selective death of human monocytes (M phi). After 30-45 minute incubations with this agent, human peripheral blood mononuclear cells (PBM) were nearly completely depleted of M phi. Associated with this M phi depletion, PBM were rendered unresponsive to a variety of T and B cell mitogens including the %plant% lectins phytohemagglutinin, concanavalin A, and pokeweed mitogen as well as the oxidative mitogens sodium periodate and neuraminidase plus galactose oxidase. Leu-OMe mediated loss of responsiveness was the result of a selective loss of an accessory cell necessary for each of these responses since reconstitution was accomplished by the addition of a M phi-enriched adherent cell population. While intact adherent cells could reconstitute responsiveness, crude M phi supernatants or highly purified human IL 1 alone were ineffective. Further identification of the Leu-OMe sensitive accessory cell indicated that it was entirely contained within the fraction of the adherent population identified by the monoclonal anti-M phi antibody, 63D3. The mechanism by which Leu-OMe Killed M phi was dependent on the %lysosomal% content of these cells, since agents that altered %lysosomal% enzyme activity such as chloroquine or NH4Cl protected M phi from Leu-OMe. Thus, the selective killing of M phi by Leu-OMe appeared to relate to the characteristically rich endowment of %lysosomes% within these cells. These results support the conclusion that a %lysosome%-rich, leucine methyl ester-sensitive, intact M phi identified by the monoclonal anti-M phi antibody 63D3 is the circulating accessory cell required for mitogen-triggered human B and T cell activation.

2/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 The Dialog Corp. All rts. reserv.

00988941 70187782
[Lymphocyte stimulation by pokeweed mitogen (PWM)]
Lymphocytenstimulierung durch Pokeweed-Mitogen (PWM)
Brittinger G; Konig E
Klin Wochenschr (GERMANY, WEST) Dec 15 1969, 47 (24) p1307-13, ISSN 0023-2173 Journal Code: KWH
Languages: GERMAN
Document type: JOURNAL ARTICLE; REVIEW
(63 Refs.)

2/7/10 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

13462930 BIOSIS Number: 99462930
The C-terminal HDEL sequence is sufficient for retention of secretory proteins in the endoplasmic reticulum (ER) but promotes vacuolar targeting of proteins that escape the ER
Gomord V; Denmat L-A; Fitchette-Laine A-C; Satiat-Jeunemaitre B; Hawes C; Faye L
LTI-CNRS URA 203, UFR Sci., IFRMP 23, Univ. Rouen, 76821 Mt. St. Aignan Cedex, France
Plant Journal 11 (2). 1997. 313-325.
Full Journal Title: Plant Journal
ISSN: 0960-7412
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 008 Ref. 118599
Proteins are co-translationally transferred into the endoplasmic reticulum (ER) and then either retained or transported to different intracellular compartments or to the extracellular space. Various molecular signals necessary for retention in the ER or targeting to different compartments have been identified. In particular, the HDEL and KDEL signals used for retention of proteins in yeast an animal ER have also been described at the C-terminal end of soluble ER processing enzymes in %plants%. The fusion of a KDEL extension to vacuolar proteins is sufficient for their retention in the ER of %transgenic% %plant% cells. However, recent results obtained using the same strategy indicate that HDEL does not contain sufficient information for full retention of phaseolin expressed in tobacco. In the present study, an HDEL C-terminal extension was fused to the vacuolar or extracellular (DELTA-pro) forms of sporamin. The resulting SpoHDEL or DELTA-proHDEL, as well as Spo and DELTA-pro, were expressed at high levels in %transgenic% tobacco cells (Nicotiana tabacum cv BY2). The intracellular location of these different forms of recombinant sporamin was studied by subcellular fractionation. The results clearly indicate that addition of an HDEL extension to either Spo or DELTA-pro induces accumulation of these sporamin forms in a compartment that co-purifies with the ER markers NADH cytochrome C reductase, binding protein (BiP) and calnexin. In addition, a significant SpoHDEL or DELTA-proHDEL fraction that escapes the ER retention machinery is transported to the vacuole. From these results, it may be proposed that, in addition to its function as an ER retention signal, HDEL could also act in quality control by targeting chaperones or chaperone-bound proteins that escape the ER to the %plant% %lysosomal% compartment for degradation.

2/7/11 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

11890815 BIOSIS Number: 98490815
Gaucher disease: Expression of active human acid beta-glucosidase in %transgenic% tobacco %plants%
Weissenborn D; Bennett S; Radin D; Ponce E; Grabowski G A; Oishi K; Cramer C L
CropTech Dev. Corp., Blacksburg, VA, USA
American Journal of Human Genetics 57 (4 SUPPL.). 1995. A38.
Full Journal Title: 45th Annual Meeting of the American Society of Human Genetics, Minneapolis, Minnesota, USA, October 24-28, 1995. American Journal of Human Genetics
ISSN: 0002-9297
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 011 Ref. 192623

2/7/12 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

9116921 BIOSIS Number: 93101921
QUANTITATIVE ULTRASTRUCTURAL EFFECTS OF CISPLATIN PLATINOL CARBOPLATIN
JM8 AND IPROPLATIN JM9 ON NEURONS OF FRESHWATER SNAIL LYMNAEA-STAGNALIS
MUELLER L J; MOORER-VAN DELFT C M; ROUBOS E W; VERMORKEN J B; BOER H H
FAC. BIOL., VRIJE UNIVERSITEIT, DE BOELELAAN 1087, 1081 HV AMSTERDAM-BUITENVELDERT, NETH.
CANCER RES 52 (4). 1992. 963-973. CODEN: CNREA
Full Journal Title: Cancer Research
Language: ENGLISH
Qualitative and quantitative ultrastructural effects of the %plantnium% compounds cisplatin (Platinol), carboplatin (JM8), and iproplatin (JM9) were studied on two types of identified peptidergic neuron (caudodorsal cells, light green cells) in the pond snail Lymnaea stagnalis. Depending on the parameter under investigation, either one or both cell types were studied. Central nervous systems of the snail were incubated for 5 and 20 h in various identical and equitoxic drug concentrations. Cisplatin had the most severe effects. Platinol, i.e., cisplatin dissolved in NaCl solution with the addition of HCl (pH 2.0-3.0), as well as cisplatin dissolved in snail Ringer's solution (pH 7.8), caused swelling of axons and distensions of the intercellular spaces. This drug induced an increase in chromatin clump size in the caudodorsal cells (20-h incubation), while carboplatin and iproplatin induced the formation of many small chromatin clumps. Incubation in snail Ringer's solution (controls) and cisplatin affect the morphology of the nucleoli. At high dosages of cisplatin, the nucleoli of light green cells were %transformed% into homogeneous dense strucures. The data indicate that platinum compounds react with nuclear and nucleolar DNA.

All three drugs affected the activity and organization of the rough endoplasmic reticulum and the Golgi apparatus of the peptidergic neurons studied (qualitative observations). These effects, which point to a reduced neuropeptide synthesis, may be secondary, i.e., exerted via inhibition of RNA synthesis and risobome formation (nucleoli). The fact that the number of neuropeptide granules in the cytoplasm of the cells remained constant (both cell types) may indicate that granule transport was also inhibited. Cisplatin and iproplatin induced an increase in the number of %lysosomes% in the light green cells. The number of lipid droplets in these cells was not affected by drug treatment. The results corroborate clinical data indicating that cisplatin is highly neurotoxic. Despite conflicting clinical data, observations on the snail neurons suggest that iproplatin is also neurotoxic, although less than cisplatin. Carboplatin is minimally neurotoxic, which is in accordance with clinical data. The central nervous system of Lymnaea is a suitable model for studying possible neurotoxic effects of platinum compounds.

2/7/13 (Item 1 from file: 10)
DIALOG(R)File 10:AGRICOLA
(c) format only 1998 The Dialog Corporation p. All rts. reserv.

3426131 20444202 Holding Library: AGL
NIH3T3 cell transfected with the yeast H+-ATPase have altered rates of protein turnover
Gunn, J.M. Martinez-Zaguilan, R.; Wald-Hopkins, S.; Woolridge, D.; Gillies, R.J.
Texas A&M University, College Station, TX.
Orlando, Fla. : Academic Press.
Archives of biochemistry and biophysics. Nov 1, 1994. v. 314 (2) p. 268-275.
ISSN: 0003-9861 CODEN: ABBIA4
DNAL CALL NO: 381 Ar2
Language: English
Includes references
Place of Publication: Florida
Subfile: IND; OTHER US (NOT EXP STN, EXT, USDA; SINCE 12/76);
Document Type: Article
NIH3T3 cells transfected with the yeast plasma membrane H+-ATPase (RN1a line) or transfected with a low-activity mutant H+-ATPase (N-Mut line) were used to examine the relationship between cytosolic pH (pHcyt) and protein turnover. At an extracellular pH (pHex) of 7.15, NIH3T3 and N-Mut cells have a pHcyt of 7-7.1 and a vacuolar pH (pHvac of 6.3, whereas in RN1a cells both the pHcyt and the pHvac are 0.3 unit more alkaline. Rates of protein synthesis and degradation are optimum at pHex 7.2 and are much more sensitive to pH changes in RN1a cells than in NIH3T3 cells. However, irrespective of pH, rates of protein degradation in RN1a cells are always less than those measured in NIH3T3 cells. Rates of protein synthesis are the same for sparse cultures of RN1a and NIH3T3 cells and show a density-dependent decline in NIH3T3 cells but remain high in RN1a cells even at high cell densities. These data indicate that the elevation of pHcyt caused by %transformation% with the H+-ATPase has no direct effect on protein synthesis. On the other hand, rates of protein degradation are consistently lower in RN1a cells than in NIH3T3 or N-Mut cells. Basal rates of protein degradation, measured in medium containing 10 mM 3-methyladenine or 10% serum or 1 micromolar insulin, as well as the autophagic response to serum or insulin withdrawal, are both significantly lower in RN1a cells. These data indicate that %transformation% with the H+-ATPase has a direct effect on rates of protein degradation, possibly through an elevation of pH. The higher pHvac will directly effect %lysosomal% protein breakdown and the higher pHcyt may be permissive for maintenance of low basal rates of protein breakdown. Overall, we conclude that %transformation% with the H+-ATPase provides a permissive environment for high rates of protein synthesis and low rates of protein degradation that result in high rates of growth and the tumor phenotype.

2/7/14 (Item 2 from file: 10)
DIALOG(R)File 10:AGRICOLA
(c) format only 1998 The Dialog Corporation p. All rts. reserv.

3261912 93012735 Holding Library: AGL
Strategies in the recognition and isolation of storage protein receptors
Hinz, G. Hoh, B.; Robinson, D.G.
Universitat Gottingen, Gottingen, FRG
Oxford : Oxford University Press.
Journal of experimental botany. Jan 1993. v. 44 (suppl.) p. 351-357.
ISSN: 0022-0957 CODEN: JEBOA6
DNAL CALL NO: 450 J8224
Language: English
In the special issue: Vesicle traffic and protein transport in %plants% and yeast / edited by D.G. Robinson, K.J. Oparka and M.D. Watson. Papers presented at an International Symposium, March 23-27, 1992, Gottingen, FRG.
Includes references.
Subfile: OTHER FOREIGN;
Document Type: Article
%Plants% do not possess the %lysosomal% mannose 6-phosphate-dependent signalling system. Therefore, there must exist a different sorting machinery for vacuolar proteins. The information necessary for correct protein targeting of these proteins seems to be located in the amino acid sequence of the protein itself, most likely expressed in the secondary or tertiary structure. In order to identify the binding sites corresponding to these ligands two different approaches can be used. The first approach in identifying the putative receptor involves the isolation of the vector organelles responsible for transporting the vacuolar protein from the Golgi apparatus (GApp) to the vacuole. These are expected to carry both the cargo (proprotein) and the receptor. We have already shown that prolegumin and provicilin are transported via clathrin coated vesicles (ccv) to the storage vacuoles of developing pea cotyledons. In further experiments we showed that prolegumin remains associated with components of the ccv coat after the membrane has been removed by detergent. The second approach is to determine the binding capacity and the number of binding sites for the ligand (i.e. the proprotein) in the GApp, followed by cross-linking of the ligand to the receptor. A prerequisite for such a study is the isolation of sufficient quantities of ligand. To this end, prolegumin has been isolated and purified from a %transgenic% yeast encoding the proprotein of the Vicia faba B-type legumin.

2/7/15 (Item 3 from file: 10)
DIALOG(R)File 10:AGRICOLA
(c) format only 1998 The Dialog Corporation p. All rts. reserv.

3181988 92036249 Holding Library: AGL
Biogenesis of the yeast vacuole (%lysosome%): mutation in the active site of the vacuolar serine proteinase yscB abolishes proteolytic maturation of its 73-kDa precursor to the 41.5-kDA pro-enzyme and a newly detected 41-kDa peptide
Hirsch, H.H. Schiffer, H.H.; Muller, H.; Wolf, D.H.
Institut fur Biochemie der Universitat Stuttgart, FRG
New York, NY : Springer-Verlag New York Inc.
European journal of biochemistry. Feb 1992. v. 203 (3) p. 641-653.
ISSN: 0014-2956 CODEN: EJBCAI
DNAL CALL NO: QP501.E8
Language: English
Includes references.
Subfile: OTHER US (NOT EXP STN, EXT, USDA; SINCE 12/76);
Document Type: Article
The codon of the catalytic serine in the active site of the vacuolar serine proteinase yscB (PrB) was changed to alanine, yielding the mutant gene prb1-Ala519. Following replacement of the wild-type PRB1 allele with prb1-Ala519, only a 73-kDa molecule was detected by immunoprecipitation with PrB-specific antiserum. The size of the mutant molecule corresponds to the unprocessed cytoplasmic precursor (pre-super-pro-PrB), as detected in sec61 mutants, when translocation into the endoplasmic reticulum is blocked. However, the mutant molecule is completely translocated into the secretory pathway, as indicated by protection from proteinase K digestion in spheroplast lysates in the absence of detergent. When N-glycosylation was inhibited in prb1-Ala519 mutant cells by tunicamycin, a smaller molecule of about 71 kDa appeared consistent with single N-glycosylation and signal-sequence cleavage of the translocated mutant PrB molecule in the endoplasmic reticulum. Thus, the active-site mutation prevents the wild-type processing of the N-glycosylated 73-kDa precursor of PrB to the 41.5 kDa pro-PrB in the endoplasmic reticulum. In order to characterize the processing of wild-type super-pro-PrB in more detail, we generated antibodies against the non-enzymatic superpeptide domain of the 73-kDa precursor expressed in Escherichia coli. We find that, in addition to pro-PrB, a distinct protein (superpeptide) with a mobility of about 41 kDa in SDS/PAGE is generated in the endoplasmic reticulum. Pulse-chase experiments indicate rapid degradation of the 41-kDa superpeptide in wild-type cells. Correspondingly, the superpeptide was virtually undetectable by immunoblotting wild-type cell extracts. In contrast, no degradation of radioactively labeled 41-kDa superpeptide was observed within 60 min in mutant strains deficient in the vacuolar proteinase yscA (PrA), in which maturation of vacuolar pro-PrB to active PrB is blocked. Accordingly, superpeptide antigenic material was readily detecte

2/7/16 (Item 1 from file: 50)
DIALOG(R)File 50:CAB Abstracts
(c) 1998 CAB International. All rts. reserv.

02761973 CAB Accession Number: 931642661
Structure, functional properties and vacuolar targeting of the barley thiol protease, aleurain.
Holwerda, B. C.; Rogers, J. C.
Division of Hematology-Oncology, Washington University School of Medicine, St Louis, USA.
Journal of Experimental Botany vol. 44 (supplement): p.321-329
Publication Year: 1993
ISSN: 0022-0957
Language: English
Document Type: Journal article
The barley vacuolar protease, aleurain, shares sequence, structural and enzymatic features with the mammalian %lysosomal% protease, cathepsin H, that are unique to the thiol protease class of enzymes. Aleurain has additional amino acid residues at the N-terminus of its propeptide that cause it to be targeted to the vacuole; two adjacent sequences, SSSSFADS and SNPIRP, are separate targeting determinants. Each, when substituted into an homologous location in the prosequence of a thiol protease that is

ordinarily secreted from %plant% cells, directed that protein to the vacuole. When the two were present together in the chimaeric protein (in %transgenic% %plants%), targeting efficiency was increased. Thus it is clear that properly folded proteins with sequences that are recognized by the mechanism for vacuolar targeting will be directed to that compartment. Evidence is presented that some small changes in the prosequence of a chimaeric protein carrying these determinants caused it to be retained in the endoplasmic reticulum, probably because it was not folded properly. With prolonged incubation, however, a portion of the misfolded protein was directed to the vacuole. This result raises the question of whether denatured proteins in the endomembrane system will also be directed to the vacuole, possibly for degradation. 38 ref.

2/7/17 (Item 2 from file: 50)
DIALOG(R)File 50:CAB Abstracts

02118905 CAB Accession Number: 890392514
Ultrastructural %transformations% in the cytoplasm of differentiating Hyacinthus orientalis L. pollen cells.
Bednarska, E.
Department of Plant Cytology and Genetics, Copernicus University, 87-100 Torun, Poland.
Acta Societatis Botanicorum Poloniae vol. 57 (2): p.235-245
Publication Year: 1988
ISSN: 0001-6977
17 pl., 1 fig.
Language: English Summary Language: polish
Document Type: Journal article
The sequence of ultrastructural changes in the cytoplasm during the successive stages of pollen grain development in H. orientalis pollen cells was studied. The cytoplasmic %transformations% of the generative cell included the elimination of plastids, increase in the number of mitochondria, assumption of a spindle shape with the aid of microtubules and the characteristic development of the vacuole system with the formation of so-called coloured bodies. The cytoplasmic %transformations% of the generative cell encompassed changes in the plastids, which began to accumulate starch soon after the cell was formed, then released it shortly before anthesis, an increase in the number of mitochondria and an increase in the number of highly active dictyosomes just before anthesis. Changes in the structure of the border region between the differentiating pollen cells were associated mainly with the periodical appearance of a callose wall and the presence of %lysosome%-like bodies in the cytoplasm of the vegetative cell surrounding the generative cell. They arose soon after the disappearance of the callose wall and disappeared shortly before anthesis. 30 ref.

2/7/18 (Item 3 from file: 50)
DIALOG(R)File 50:CAB Abstracts

00381886 CAB Accession Number: 750740127
Existence of membrane-like %lysosomal% formations in %plant% cells.
Herich, R.; Bonak, M.
Dep. of Pl. Physiol., Comenius Univ., Bratislava, Czechoslovakia.
Zeitschrift fur Pflanzenphysiologie vol. 75 (5): p.457-459
Publication Year: 1975
Language: English
Document Type: Journal article
Electron microscope studies of %transformation% of the membrane-like complex of the endoplasmic reticulum into a %lysosomal% formation in meristematic cells of Vicia faba root tips are described. 6 ref.

2/7/19 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

9969222 EMBASE No: 96133788
Changes in ultrastructure of cytoplasm and nucleus during spermiogenesis in Chara vulgaris
Kwiatkowska M.
Dept. Cytophysiology, University of Lodz, Pilarskiego 12/14, 90-231 Lodz Poland
Folia Histochemica et Cytobiologica (Poland), 1996, 34/1 (41-56)
CODEN: FHCYE ISSN: 0015-5586
LANGUAGES: English SUMMARY LANGUAGES: English
In the present study much attention was paid to the first and middle stages of spermiogenesis in Chara vulgaris. The spermiogenesis was divided into 8 phases (A-H). In telophase leading to spermatid formation (A phase) there are no structural changes, indicating that cells pass into a new functional stage - spermiogenesis. B phase: After the formation of a posttelophase nucleus, the difference is striking in chromatin of newly formed spermatids and chromatin nuclei in cycling cells. The nuclei of spermatids form big clusters of dense chromatin and nucleoli remain as in telophase. However, in cycling cells condensed chromatin forms fine reticulum while nucleoli contain abundant granular component. C phase: The movement of the nucleus to the side wall, characteristic for early spermiogenesis, is not preceded by changes in the structure of the nucleus. D phase: In D phase and later free spaces between plasmalemma and the cell wall appear. In these spaces two flagella have a typical structure (9+2). They are surrounded by plasmalemma with rhombus-shaped scales on its surface. The structure of nucleus is characterised by a thick, dense layer of chromatin and gradual disappearance of nucleoli by extrusion to the cytoplasm. In electron-transparent ground cytoplasm, numerous ribosomes forming clusters, spirals and chains are present. Numerous rough ER cisternae with light content also appear. Bodies similar to secondary %lysosomes% and intensified activity of Golgi structures are observed. E phase: Large amounts of proteins seem to be synthesized and accumulated in rough ER cisternae which are filled with an electron dense substance. The same kind of substance can be seen within the perinuclear space. One may assume that proteins migrate through the nuclear envelope to the cell nucleus. Probably at that moment the main proteins taking part in the reorganisation of chromatin structure and in the exchange of somatic proteins into generative ones are formed. Simultaneously synthesis of other types of proteins continues. Active Golgi structures producing numerous light and coated vesicles complete the picture of intensive metabolism. Parallelly reduction of cytoplasm takes place. F phase: The nuclear chromatin becomes netlike after DNP staining, without a thick layer of condensed chromatin close to the nuclear envelope. Simultaneously, all types of structures with positive contrast after EDTA migrate polarly from nucleus to the cytoplasm. Further reduction of cytoplasm takes place and protein synthesis continues as suggested by the presence of numerous free polysomes. G phase: The structure of chromatin fibrils undergoes a complete %transformation% . They become much thicker, parallel to each other, changing the orientation along with the formation of nucleus coils. The nucleus is devoid of most nucleoplasm structures. It has significantly elongated shape and shows the presence of manchette microtubules on the outside of nuclear envelope and lamina attached to the inner membrane of nuclear envelope. Condensed mitochondria are located near flagella and nucleus while plastids with starch grains lined up on the opposite side of the spermatozoid are also surrounded by microtubules. H phase: Nuclear fibrils form lamellar interconnections and the nucleus has a form of dense reticular structure surrounded by the nuclear envelope without pores.

2/7/20 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

9439716 EMBASE No: 95008660
The expression and processing of human beta-amyloid peptide precursors in Saccharomyces cerevisiae: Evidence for a novel endopeptidase in the yeast secretory system
Hines V.; Zhang W.; Ramakrishna N.; Styles J.; Mehta P.; Kim K.S.; Inuis M.; Miller D.L.
Department of Microbial Expression, Chiron Corp., Emeryville, CA 94608 USA
CELL. MOL. BIOL. RES. (United Kingdom), 1994, 40/4 (273-284) CODEN: CMBRE ISSN: 0968-8773
LANGUAGES: English SUMMARY LANGUAGES: English
In mammalian cells, the transmembrane beta-amyloid peptide precursor (beta-APP) undergoes a complex series of alternative proteolytic processing steps that result in the secretion of varying proportions of its extra-cellular domain (protease nexin II) and beta-amyloid peptide. The protein is also reinternalized and degraded in the endosomal-%lysosomal% system. The relative efficiencies of these competing processes determine the yield of beta-amyloid peptide. Several proteases have been implicated in this complex processing pathway, although none has been identified to date. The yeast secretory system contains proteases homologous to mammalian pro-hormone convertases and is susceptible to genetic manipulation. We therefore investigated the expression and processing of the beta-amyloid peptide precursors (beta-APP-695 and beta-APP-751) in Saccharomyces cerevisiae %transformed% with human beta-APP cDNA's. beta-APP (695 or 751) cDNA either with its authentic signal sequence or the yeast-derived prepro-alpha-factor leader, was inserted into a glucose-regulated expression vector and transfected into a protease-deficient yeast strain. In all instances, expression of beta-APP was about 1% of total protein. Protease protection studies indicated that either the natural human signal sequence or the alpha-factor leader sequence targetted beta-APP to the endoplasmic reticulum and inserted it with the amino-terminal domain in the lumen. All of the beta-APP fused to the alpha-factor leader proceeded to the trans-Golgi, where Kex2 endopeptidase removed the leader and released the normal amino-terminus of beta-APP. About one-half of the beta-APP was also cleaved at the 'alpha-secretase' site in the middle of the beta-peptide sequence, 12 residues before the membrane-spanning sequence. A fraction of the alpha-secretase-cleaved beta-APP appeared in the culture medium; however, most of it associated with the exterior of the cells. The carboxyl-terminal fragments formed by cleavage at the alpha-secretase site accumulated in the membranes. Other proteolytic processes generated membrane-associated carboxyl-terminal fragments that also resembled those found in mammalian cells. These results indicate that the secretory system of S. cerevisiae possesses proteases with specificities similar to the mammalian enzymes that process beta-APP.

2/7/21 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

6276917 EMBASE No: 87013542
Down-regulation of interleukin 1 (IL 1) receptor expression by IL 1 and fate of internalized sup 1sup 2sup 5I-labeled IL 1beta in a human large granular lymphocyte cell line
Matsushima K.; Yodoi J.; Tagaya Y.; Oppenheim J.J.
Laboratory of Molecular Immunoregulation, Biological Response Modifiers Program, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Frederick Cancer Research Facility, Frederick, MD 21701-1013 USA
J. IMMUNOL. (USA), 1986, 137/10 (3183-3188) CODEN: JOIMA
LANGUAGES: ENGLISH
The regulation of interleukin 1 (IL 1) receptor expression on a human large granular lymphocyte cell line, YT, and fate of internalized sup 1sup 2sup 5I-labeled IL 1beta (sup 1sup 2sup 5I-IL 1beta) were studied. YT cells were selected for this study, because this cell line expresses a large number of specific high-affinity receptor for IL 1, responds biologically to exogenously added IL 1 by expressing high-affinity IL 2 receptors, and does not produce IL 1. YT cells constitutively express approximately 7 x 10sup 3 IL 1 receptors/cell with a Kd approx. 10sup -sup 1sup 0 M. Neither IL 2, phorbol myristic acid, nor lipopolysaccharide affected the total binding of sup 1sup 2sup 5I-IL 1beta by YT cells. In contrast, the capacity of YT cells to bind sup 1sup 2sup 5I-IL 1beta when incubated at 37degr.C for 3 to 16 hr with a low dose of purified IL 1beta (approx. 6 U/ml) was reduced by > 80%. The loss of binding capability gradually recovered by 16 hr after removal of IL 1beta from cultured YT cells. The apparent loss of IL 1 receptor expression was accompanied by the internalization of sup 1sup 2sup 5I-IL 1beta into cells. Acid treatment of YT cells to remove bound sup 1sup 2sup 5I-IL 1beta at 4degr.C showed that 50% of the sup 1sup 2sup 5I-IL 1beta bound to cells could no longer be recovered after 30 min at 37degr.C, and this increased to 80% after 3 hr at 37degr.C. Fractionation of cell extracts on Percoll gradient additionally showed sup 1sup 2sup 5I-IL 1beta to appear intracellularly after receptor binding on plasma membranes, and to be successively transferred to some membranous organelles (d congruent with 1.037) through an intermediate density organelle (d congruent with 1.050), and to finally end up in %lysosomal% cell fractions (d congruent with 1.05 to 1.08) after approximately 3 hr at 37degr.C. Only approx. 5% of internalized sup 1sup 2sup 5I-IL 1beta was released into culture media by 6 hr of incubation at 37degr.C. However, the radioactivity in the TCA soluble fraction of the culture media increased gradually by 6 hr and a %lysosomotropic% enzyme, ethylamine, significantly inhibited both the transfer of internalized sup 1sup 2sup 5I-IL 1beta to the %lysosomal% fraction and the degradation of sup 1sup 2sup 5I-IL 1beta. This study represents the first evidence of autoregulation of IL 1 receptors by IL 1 and internalization of IL 1 molecules after binding to receptors. This observation suggests that the low number of receptors for IL 1 on many cell types may be attributable to persistent down-regulation by low levels of exogenous IL 1.

2/7/22 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

6250733 EMBASE No: 86245796
Evaluation of ricin A-chain immunotoxins directed against human T cells
Press O.W.; Vitetta E.S.; Farr A.G.; et al.
Fred Hutchinson Cancer Research Center, Division of Oncology, Department of Medicine, University of Washington, Seattle, WA 98104 USA
CELL. IMMUNOL. (USA), 1986, 102/1 (10-20) CODEN: CLIMB
LANGUAGES: ENGLISH
We have synthesized four immunotoxins (ITs) by covalently coupling the A chain of ricin to murine monoclonal antibodies that recognize surface antigens on human T cells. Treatment of human peripheral blood lymphocytes with either 10.2-A, directed against the CD5 (Tp67) antigen, or 64.1-A, directed against the CD3 (Tp19) antigen, abolished protein synthesis in cells subsequently cultured with phytohemagglutin (PHA). In contrast, two other ITs (9.6-A and 35.1-A), both directed against the CD2 (Tp50) antigen, and minimal effects on protein synthesis in PHA-stimulated cells. The binding of each IT to T cells was shown by immunofluorescence with fluorescein-conjugated goat anti-mouse immunoglobulin (FITC-GAMIg) and fluorescein-conjugated rabbit anti-ricin A-chain (FITC-RAR) antibodies. Activity of the ricin A chain in each IT was demonstrated by its ability to inhibit protein synthesis in a cell-free reticulocyte lysate assay. Ultrastructure immunoperoxidase analysis of IT internalization showed that ineffective and effective ITs were endocytosed at the same rate (50% of cells had labeled endosomes after 15 min). However, ineffective IT 35.1-A was more rapidly delivered to %lysosomes% (15-30 min) than effective ITs (10.2-A and 64.1-A) (> or = 30 min). The data support the hypothesis that there are several distinct pathways for internalization of ITs and that the ability of ricin A chain to reach and inactivate ribosomes may depend upon the specific membrane receptor involved in binding a given IT, its route of internalization, and the rate of entry of the IT into %lysosomes%.

2/7/23 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

5961668 EMBASE No: 85207178
Distinct differentiation-inducing activities of gamma-interferon and cytokine factors acting on the human promyelocytic leukemia cell line HL-60
Harris P.E.; Ralph P.; Gabrilove J.; et al.
Department of Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, New York, NY 10021 USA
CANCER RES. (USA), 1985, 45/7 (3090-3095) CODEN: CNREA
LANGUAGES: ENGLISH
The human promyelocytic leukemia cell line HL-60 and monoblastic leukemia cell line U937 undergo differentiation when induced by lymphokine and cytokine preparations. Growth inhibition, acquisition of immunoglobulin Fc receptors, increased expression of monocyte-related surface antigens, and an increase in %lysosomal% enzyme contents accompany maturation induced by gamma-interferon and other cytokine factors tested. Additionally, increased receptors for chemotactic peptide (fMLPR), increased hydrogen peroxide release in response to phorbol myristic acetate stimulation, and the release of prostaglandins (PGEsub 2 and 6-keto-PGF(1a)) follow exposure to lymphokine and cell line sources of myeloid colony-stimulating activity (CSA). gamma-Interferon (gamma-IFN) induced fMLPR in HL-60 (only at 1000 units/ml) but not in U937. Additionally, gamma-IFN did not induce prostaglandin release in either cell line. These myeloid colony-stimulating activity-associated differentiation-inducing factors were obtained from the human hepatoma cell line SK-Hep and bladder carcinoma cell line 5637, which were free of interferon activity. The 2-day phytohemagglutinin-induced lymphokine contained no detectable CSA and was a good source of differentiation activity. A simple, rapid assay for a new human CSA with pluripotent hematopoietic stimulating activity (pluripoietin) is described based on stimulation of (sup 3H)glucosamine incorporation. Cell line conditioned media containing pluripoietin, purified pluripoietin, and gamma-IFN are active in this assay. These myeloid leukemia cell line differentiation factors are thus different from interferon and conventional CSA. These results suggest that endogenous human cytokines may have a role in the differentiation of leukemic as well as normal myeloid cells.

2/7/24 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

5686971 EMBASE No: 84182637
Interference of cyclosporin with lymphocyte activation: Blockage of the mitogen-induced increases of %lysosomal% and mitochondrial activities
Koponen M.; Grieder A.; Loor F.
Institut fuer Klinische Immunologie, Inselspital, CH 3010 Bern SWITZERLAND
IMMUNOLOGY (ENGLAND), 1984, 53/1 (55-62) CODEN: IMMUA
LANGUAGES: ENGLISH
Mouse lymphocytes were activated by a mitogenic dose of concanavalin A and analysed by flow cytometry to monitor the increases of mitochondrial activity (using rhodamine 123 as probe) and of %lysosomal% activity (using euchrysin (acridine orange) as probe). Cyclosporin A-treated lymphocytes were not capable of responding to concanavalin A in the same way as untreated lymphocytes: both the increased uptakes of rhodamine 123 by mitochondria and of acridine orange by %lysosomes% were strongly diminished, though not abolished. Cyclosporin may thus interfere at a step of activation prior or concurrent to those early changes of lymphocyte physiology. It looks like that it allows mitogen-activated cells to go through part of the mitochondrial maturation which precedes initiation of nuclear DNA synthesis, after which the cells remain blocked at that incomplete maturation level.

2/7/25 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

5496326 EMBASE No: 83248149
Neutrophil-assisted DNA synthesis by human lymphocytes in response to mevalonic acid; enhancement by cytochalasin B
Larson R.A.; Gordon L.I.; Yachnin S.
Dep. Med., Univ. Chicago Sch. Med., Chicago, IL 60637 USA
CELL. IMMUNOL. (USA), 1983, 81/2 (357-372) CODEN: CLIMB
LANGUAGES: ENGLISH
Mevalonic acid is capable of initiating DNA synthesis, morphologic %transformation%, and cell division in cultures of human peripheral blood lymphocytes. Pure populations of lymphocytes respond poorly to mevalonic acid, but their response can be enhanced by peripheral blood neutrophils. Addition of cytochalasin B (0.5-1.0 mug/ml), but not cytochalasin A, to mixed neutrophil-lymphocyte cultures enhances the response of lymphocytes to both Con A and mevalonate, but the increment in mevalonate-induced DNA synthesis (+343%) far exceeds the enhancement which cytochalasin B produces in the Con A response (+24%). As a consequence, the DNA synthetic response in mevalonate (10sup -sup 2 M) containing cultures averages 39% of the response to an optimal dose of Con A. The cytochalasin B-enhanced response of mixed neutrophil-lymphocyte cultures to mevalonate is abolished by prior X irradiation of the lymphocytes, or their pretreatment with mitomycin C, as well as by the addition of hydroxyurea to the cultures but is not altered by prior X irradiation or mitomycin C pretreatment of the neutrophil helper population. These experiments suggest that the enhancing effect of cytochalasin B in the response of mixed neutrophil-lymphocyte

cultures to mevalonic acid results from its ability to potentiate a time-dependent conditioning effect on lymphocytes which neutrophils exert. The conditioning effect of neutrophils cannot be achieved by cell-free neutrophil %lysosomal% enzymes released by exocytosis, and reactive oxygen species potentially generated by neutrophils are not involved. Attempts to demonstrate the production by neutrophils of a soluble mediator induced by mevalonate in the presence of cytochalasin B were without success. In the presence of cytochalasin B, only the metabolically active R(-) enantiomeric form of mevalonate is capable of initiating DNA synthesis in mixed neutrophil-lymphocyte cultures. The cytochalasin B-potentiated response of mixed neutrophil-lymphocyte cultures to mevalonic acid is preferentially displayed in cultures containing E-rosette-negative, as opposed to E-rosette-positive, lymphocytes. These observations add to the growing knowledge about the relationship between mevalonate metabolism, DNA synthesis, and cell replication.

2/7/26 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

5433790 EMBASE No: 83185613
Spontaneous in vitro malignant %transformation% in a Xeroderma pigmentosum fibroblast line
Thielmann H.W.; Fischer E.; Dzarlieva R.T.; et al.
Inst. Biochem., Ger. Cancer Res. Cent., 6900 Heidelberg GERMANY, WEST
INT. J. CANCER (SWITZERLAND), 1983, 31/6 (687-700) CODEN: IJCNA
LANGUAGES: ENGLISH
This paper deals with a spontaneous malignant %transformation% in one of our XP fibroblast lines. This cell line, designated XP29MA, was derived from a 14-year-old boy who did not show skin tumors or precancerous alterations either at the time of clinical examination or when the biopsy was taken. We have compared the following features in both the malignant and the benign cell line from which the malignant line developed: tumor formation in nude mice, repair capacity, cytogenetic status, light and electron microscopic characteristics. The benign cell line XP29MA had a doubling time of 4.3 d, did not form tumors in nude mice, showed a very low repair capacity (as determined by colony-forming ability, unscheduled DNA synthesis and alkaline elution) but exhibited a normal cytogenetic and ultrastructural status. In contrast, the %transformed% cell line XP29MAmal grew three times faster, formed colonies in methyl cellulose, gave rise to fibrosarcomas in nude mice, showed a drastically higher repair capacity, and was characterized by an extreme genetic imbalance, resulting from numerical and structural chromosome alterations of Nos. 1, 3, 4, 8, 12, 16, 17, 18, 20 and 21. Ultrastructural examination revealed fusiform and polygonal cells, the latter exhibiting large indented nuclei, vesicular dilatations of the endoplasmatic reticulum and numerous %lysosomes%. The higher repair capacity in XP29MAmal cells is tentatively explained in terms of reversion, enhancement of post-replication repair and/or expression of SOS-type functions.

2/7/27 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

1620932 EMBASE No: 80122669
Cytophilic binding of IgE to the macrophage. III. Involvement of cyclic GMP and calcium in macrophage activation by dimeric or aggregated rat myeloma IgE
Dessaint J.P.; Waksman B.H.; Metzger H.; Capron A.
Dept. Pathol., Yale Univ. Sch. Med., New Haven, Conn. 06520 USA
CELL. IMMUNOL. (USA), 1980, 51/2 (280-292) CODEN: CLIMB
LANGUAGES: ENGLISH
Discharge of %lysosomal% enzymes, measured by release of beta-glucuronidase, was studied in uninduced rat macrophages stimulated in vitro with rat monoclonal IgE (IR 162) in different states of aggregation. Monomeric IgE showed negligible activity, while dimeric and aggregated IgE were shown to induce a rapid and selective release of beta-glucuronidase as well as new synthesis of the enzyme, without change in the cytoplasmic marker, leucine aminopeptidase. %Lysosomal% enzyme release is related to the dose of dimeric IgE, becoming maximal above 2.5 mug/ml. beta-Glucuronidase release from macrophages by dimers is competitively inhibited by monomeric IgE but only at high ratios, approximately 100-fold greater than those needed to block mast cell release of the same enzyme. The difference in inhibitability is consistent with the difference in binding affinity of macrophages and mast cells for monomeric IgE. This observation rules out the participation of the few remaining mast cells contained in the macrophage monolayer in beta-glucuronidase release. Dimeric or aggregated IgE produced a rise in cyclic GMP coincident with the peak fixation of IgE by macrophages. Elevation of cyclic GMP by pharmacological means also stimulated beta-glucuronidase release and new synthesis, as well as enhancing the effect on these of aggregated IgE. Enzyme release by IgE did not occur in the absence of extracellular calcium. We conclude that IgE, which has been cross-linked to form dimers before binding to specific macrophage receptors, triggers the cell and that cyclic GMP (and perhaps calcium) modulates the early step of macrophage activation.

2/7/28 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

1521987 EMBASE No: 80022265
Effects of bacterial endotoxin on %lysosomal% and mitochondrial enzyme activities of established cell cultures
McGivney A.; Bradley S.G.
Dept. Microbiol., Virginia Commonwlth Univ., Richmond, Va. 23298 USA
RES J. RETICULOENDOTHEL. SOC. (USA), 1979, 26/3 (307-316) CODEN: RESJA
LANGUAGES: ENGLISH
Escherichia coli 0127:B8 lipopolysaccharide (LPS) (Westphal preparation) elicited enhanced beta-glucuronidase and acid phosphatase activities in a %lysosomal% fraction of normal WI-38 or Vero cells, but not that of %transformed% HEp-2, P388D1 or HEMS cells. Elevated %lysosomal% enzyme activity developed within 4 hr after exposure to 10 mug LPS/ml and in the absence of added serum. The increase was prevented by actinomycin D or cycloheximide. The activities of malate dehydrogenase, succinate dehydrogenase, and adenylate kinase in a mitochondrial fraction of Vero cells decreased within 2 hr after exposure to 10 mug LPS/ml. The LPS at 10 mug LPS/mg protein enhanced loss of these 3 enzyme activities from the granular portion of the mitochondrial fraction within 45 min. Bacterial endotoxin acts directly on normal established cell cultures, causing early changes in mitochondria.

2/7/29 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

734329 EMBASE No: 77114467
Ultrastructures of blastoid %transformed% lymphocytes, stimulated by several antigens
Yamada M.; Yoshinaga H.
Dept. Dermatol., Osaka Red Cross Hosp., Osaka JAPAN
J.DERM. (TOKYO) (JAPAN), 1976, 3/3 (89-96) CODEN: JDMYA
LANGUAGES: ENGLISH
Lymphocytes %transformed% into large cells with specific antigens and a non specific stimulant agent, PHA, were studied by electron microscopy. The large cells stimulated by specific antigens, i.e. tuberculin (PPD), trichophytin, sporotrichin, potassium dichromate, and cobalt chloride, were ultrastructurally different from the PHA %transformed% cells. The latter had poor organelles in the relatively narrow cytoplasmic spaces, resembling the immature lymphocytes reported by other authors, while in the wide cytoplasm of the former were numerous endoplasmic reticula, various dense bodies and %lysosome% like structures. They were similar to macrophages. Cells %transformed% by PPD showed both acid phosphatase activity and India ink phagocytizing activity.

2/7/30 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

604669 EMBASE No: 76191076
Potentiation of the T lymphocyte response to mitogens: relationship between LAF production and 'activation' of macrophages
Gery I.; Wiener E.
Dept. Med. Ecol., Hebrew Univ., Hadassah Med. Sch., Jerusalem ISRAEL
RES (N.Y.) (USA), 1975, 18/4 (252-259) CODEN: RESJA
LANGUAGES: ENGLISH
Cultured mouse peritoneal macrophages stimulated by various agents were assayed for their secretion of lymphocyte activating factor (LAF) and their degree of 'activation', evaluated by their levels of 2 %lysosomal% enzymes, acid phosphatase and beta-N-acetylglucosaminidase. No direct correlation could be found. Macrophages cultured in the presence of the potent activator, newborn calf serum, exhibited high activities of intra and extracellular enzymes, but their supernatants (SUP's) showed low LAF activity. On the other hand, cells incubated without serum had low enzyme levels, while high LAF activity was found in their SUP's. The addition of the mitogen concanavalin A resulted in increased levels of LAF, but lacked any effect on the %lysosomal% hydrolases. The levels of LAF in undiluted SUP's from endotoxin stimulated cultures were relatively low. When diluted, however, their LAF activity was found to be higher than those of SUP's from other experimental cultures. Macrophages activated by intraperitoneal administration of thioglycollate, known to contain high levels of %lysosomal% enzymes, did not release increased amounts of LAF. These data thus indicate that the release of LAF is not directly related to the process of conventional 'activation' of macrophages.

2/7/31 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

381630 EMBASE No: 75176908
Enzyme patterns in non neoplastic and spontaneously %transformed% tissue culture cells: a histochemical and biochemical study
Wilson P.D.
Dept. Cell. Pathol., Imp. Cancer Res. Fund, London UNITED KINGDOM

J.PATH. (SCOTLAND), 1974, 114/1 (21-28) CODEN: JPBAA
LANGUAGES: ENGLISH
Enzyme patterns were compared by quantitative biochemical assay and optical and electron microscope histochemistry of 7 spontaneously %transformed% neoplastic and 5 non neoplastic long term tissue culture cell lines with similar morphologic characteristics although derived from various organs of young, old and embryo C57 and C3H mice. The activity of surface enzymes was strikingly changed in neoplastic lines. Alkaline phosphatase was absent or at very low levels, G6PDH, LDH and 5' nucleotidase levels were low and beta glucuronidase levels were high in neoplastic lines compared with non neoplastic lines. Acid phosphatase was present in %lysosomes% but was also demonstrated on the plasma membranes of 4 tumor producing and 4 non tumor producing cell lines.

2/7/32 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

333181 EMBASE No: 75126129
Biological effects of scarlet fever toxin and the role of activation of lymphocytes
Hribalova V.
Inst. Hyg. Epidemiol., Prague CZECHOSLOVAKIA
J.HYG.EPIDEMIOL. (PRAHA) (CZECHOSLOVAKIA), 1974, 18/3 (297-301)
CODEN:
JHEMA
LANGUAGES: ENGLISH
It may be suggested that the lymphocyte stimulating activity of erythrogenic toxin has immunological consequences analogous to those demonstrated for nonspecific mitogens. A subject of theoretical speculation is the issue to what extent the metabolic consequences of lymphocyte stimulation, i.e., the possible rise of the level of %lysosomal% enzymes and the production of a number of biologically active mediators of cellular immunity, may contribute, on the one hand, to the increased sensitivity of the organism to other toxic substances and, on the other hand, possibly to the development of the tissue lesions encountered in the so called delayed sequelae of streptococcal infections.

2/7/33 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1998 Derwent Publ Ltd. All rts. reserv.

211876 DBA Accession No.: 97-06997 PATENT
Inhibiting infection of eukaryotic cells by microorganisms - microorganism e.g. HIV virus-1 or HIV virus-2 receptor fusion protein gene expression in %transgenic% animal or %transgenic% %plant% for disease-resistance
AUTHOR: Russell S J
CORPORATE SOURCE: London, UK.
PATENT ASSIGNEE: Med.Res.Counc. 1997
PATENT NUMBER: WO 9713856 PATENT DATE: 970417 WPI ACCESSION NO.: 97-235892 (9721)
PRIORITY APPLIC. NO.: GB 9520641 APPLIC. DATE: 951010
NATIONAL APPLIC. NO.: WO 96GB2465 APPLIC. DATE: 961009
LANGUAGE: English
ABSTRACT: A new method of inhibiting intracellular infection of a eukaryotic cell by a microorganism (preferably HIV virus-1 or HIV virus-2) involves introducing into the eukaryotic cell a nucleic acid sequence directing the expression of a chimeric protective protein (PP) receptor molecule (consisting of an effective portion of the binding domain of the natural receptor for the microorganism) on the surface of the cell. The PP has high binding affinity for a component of the microorganism, and binding of the PP to the microorganism prevents it infecting the cell. Binding of the microorganism to the PP directs it to the endosomal compartment of the host cell. The PP consists of a %lysosomal% targeting signal, directing bound microorganisms to a %lysosomal% compartment for degradation. The PP is expressed at a level sufficient so there is a greater number of PP sites on the surface of the cell than natural binding sites for the microorganism. It also projects further from the cell surface than the natural receptor. A %transgenic% %plant% or animal expressing the PP receptor and having increased resistance to a disease caused by a pathogenic microorganism is claimed. (20pp)

2/7/34 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1998 Derwent Publ Ltd. All rts. reserv.

210819 DBA Accession No.: 97-05940 PATENT
Production of enzymatically active (modified) %lysosomal% enzyme in %transgenic% %plants% - human recombinant native and mutant %lysosome% enzyme preparation by plasmid expression in tobacco %transgenic% %plant%
AUTHOR: Radin D N; Cramer C L; Oishi K K; Weissenborn D L
CORPORATE SOURCE: Blacksburg, VA, USA.
PATENT ASSIGNEE: Virginia-Tech.Intellectual-Prop.; Croptech-Development 1997
PATENT NUMBER: WO 9710353 PATENT DATE: 970320 WPI ACCESSION NO.: 97-202248 (9718)
PRIORITY APPLIC. NO.: US 3737 APPLIC. DATE: 950914
NATIONAL APPLIC. NO.: WO 96US14730 APPLIC. DATE: 960913
LANGUAGE: English
ABSTRACT: A new method for producing an enzymatically active %lysosomal% enzyme or modified %lysosomal% enzyme in a %transgenic% %plant%, preferably tobacco (Nicotiana tabacum), involves growing a %transgenic% %plant% which has a recombinant expression construct consisting of a nucleotide sequence encoding the %lysosomal% enzyme, and a promoter to enable its expression by the %plant%. The %lysosomal% enzyme can then be recovered from an organ of the %transgenic% %plant%; a leaf, stem, root, flower, fruit or seed. The %lysosomal% enzyme or modified %lysosomal% enzyme is preferably a human %lysosomal% enzyme or modified human %lysosomal% enzyme, and especially a glucosylceramidase (EC-3.2.1.45), modified glucosylceramidase, L-%iduronidase% (EC.3.2.1.76) or modified L-%iduronidase%. The modified enzyme has the protein sequence of the native enzyme with one or several amino acid substitutions, additions and/or deletions; and contains a detectable marker peptide. The promoter has a specified 463 bp sequence and is inducible in the %transgenic% %plant% before or after it is harvested. Also claimed is plasmid pCTProl:hGC:FLAG (ATCC 97277, plasmid pCT22 (ATCC 97701) and plasmid pCT54. (111pp)

2/7/35 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1998 Derwent Publ Ltd. All rts. reserv.

116013 DBA Accession No.: 91-03655
Newly developed fusogenic liposome - with functionalized polyethylene glycol-lipid for e.g. carrot protoplast %transformation% (conference abstract)
AUTHOR: Sunamoto J; Akiyoshi K; Tanaka K; Sato T
CORPORATE SOURCE: Department of Polymer Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Yoshida Hommachi, Kyoto 606, Japan.
JOURNAL: Abstr.Pap.Am.Chem.Soc. (200 Meet., Pt.2, POLY44) 1990
CODEN: ACSRAL
LANGUAGE: English
ABSTRACT: In drug delivery systems (DDS) and/or cell modification, liposomes have been widely accepted as vehicles for delivery of various substances, e.g. DNA, RNA, enzymes or drugs, into cells. In the internalization of liposomes into cells, 2 possible pathways, phagocytosis and fusion, have been considered. However, in order for biologically unstable compounds to be internalized in cells, fusion is more favorable, because the liposome-loading compounds are directly delivered into the cytosol, and are able to avoid destruction by %lysosomal% enzymes. From this viewpoint, therefore, several methodologies have been proposed for making liposomes fusogenic to an intact cell. All the methodologies previously proposed, however, still have some disadvantages. In order to overcome these disadvantages, a fusogenic liposome, containing an artificial lipid (PEG-lipid), was developed, and fusogenicity of such a functionalized liposome to carrot (Daucus carota) protoplasts and conventional liposomes without PEG lipid was studied. Effective fusion was observed when 23 mol% PEG-lipid-containing egg lecithin liposomes were used. (0 ref)

06feb98 15:40:48 User219511 Session D411.4
$0.06 0.002 Hrs File155
$1.80 9 Type(s) in Format 7
$1.80 9 Types
$1.86 Estimated cost File155
$0.24 0.004 Hrs File5
$4.35 3 Type(s) in Format 7
$4.35 3 Types
$4.59 Estimated cost File5
$0.15 0.005 Hrs File10
$3.60 3 Type(s) in Format 7
$3.60 3 Types
$3.75 Estimated cost File10
$0.15 0.005 Hrs File50
$4.20 3 Type(s) in Format 7
$4.20 3 Types
$4.35 Estimated cost File50
$2.70 0.030 Hrs File73
$26.60 14 Type(s) in Format 7
$26.60 14 Types
$29.30 Estimated cost File73
$0.14 0.001 Hrs File357
$6.00 3 Type(s) in Format 7
$6.00 3 Types
$6.14 Estimated cost File357
OneSearch, 6 files, 0.050 Hrs FileOS
$0.15 FTSNET
$50.14 Estimated cost this search
$52.37 Estimated total session cost 0.127 Hrs.
Logoff: level 98.01.01 D 15:40:48

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

2-83

Requestor's Name: _____ Serial Number: _____

Date: _____ Phone: _____ Art Unit: _____

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

STAFF USE ONLY

Date completed: 2/5/98

Searcher: Stepjane

Terminal time: _____

Elapsed time: _____

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC
_____ CM-1
_____ Pre-S

Type of Search

_____ N.A. Sequence
_____ A.A. Sequence
_____ Structure
_____ Bibliographic

Vendors

_____ IG
_____ STN
_____ Dialog
_____ APS
_____ Geninfo
_____ SDC
_____ DARC/Questel
_____ Other

PTO-1590 (9-90)